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Case Report

Outbreak of multidrug-resistant tuberculosis in an aboriginal family in eastern Taiwan

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ABSTRACT

Spread of multidrug-resistant tuberculosis (MDR-TB) strains in the general population presents a serious threat to public health and severely threatens existing control efforts. Techniques such as spoligotyping and *Mycobacterium* interspersed repetitive units—variable-number tandem-repeat typing of mycobacterial isolates have been employed to confirm familial outbreaks of MDR-TB. We diagnosed and traced four MDR-TB cases in a family via genotyping. Despite aggressive treatment, the index case remained culture positive, but the other patients were cured. This is the first documentation of a familial MDR-TB outbreak affecting human immunodeficiency virus-seronegative patients in eastern Taiwan. Molecular techniques are important in the identification of sources of MDR-TB infections. The adult index case in our study developed MDR-TB due to poor compliance with the drug regimen (acquired resistance), followed by transmission of MDR-TB to his children in close household contact. This emphasizes the importance of an effective drug delivery program, such as directly observed treatment, to improve drug compliance and prevent the emergence of drug-resistant cases.

1. Introduction

The World Health Organization estimated that the incidence of multidrug-resistant tuberculosis (MDR-TB), defined as isolates with resistance to at least isoniazid and rifampicin, was 220,000–400,000 cases (best estimate, 310,000) in the year 2011. MDR-TB has become an important issue in the management of TB [1]. The spread of MDR-TB strains in the general population presents a serious threat to public health and severely threatens existing control efforts, because the treatment of MDR-TB is prolonged (18–24 months), less efficacious (success rate <60%), more toxic, and much costlier [2] than that of drug-susceptible tuberculosis.

MDR-TB can result from new transmission of a resistant strain (primary transmission) or poor management of a patient infected with drug-susceptible organisms (acquired resistance). Outbreaks of MDR-TB have occurred in health care facilities and institutional settings, primarily involving patients infected with the human immunodeficiency virus (HIV) [3–5]. A combination of epidemiologic investigation and genotyping has been used to find the origin of outbreaks and track dissemination of MDR-TB strains. In this report, we describe four HIV-seronegative MDR-TB cases in an aboriginal family in eastern Taiwan.

2. Case Reports

2.1. Case 1

The index case (Case 1) was an aboriginal man who was a tunnel worker. He lived in the village of Wan-Rong, Taiwan which had a TB incidence of 512.5 cases per population of 100,000 in 2006. He was first diagnosed with pulmonary TB in November 2000, when he was 43 years old. Sputum smears were positive for acid-fast bacilli, and sputum cultures grew *Mycobacterium tuberculosis*. This isolate was sensitive to all first-line drugs. The patient was cured after 8 months of standardized treatment, but due to a relapse in February 2002, antituberculosis treatment was restarted.

Conflicts of interest: none.

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During the second treatment course, the patient showed poor compliance with the treatment regimen. Sputum cultures were again positive in April 2004, and chest radiography revealed worsening of left lung infiltrations and cavitations (Fig. 1A). The results of a drug-susceptibility test (DST) of the sputum culture 2 months later revealed resistance to isoniazid (H) and rifampicin (R), so the patient's regimen was changed to ethambutol (E), pyrazinamide (Z), streptomycin (S), prothionamide (Pto), and moxifloxacin (Mfx). In September 2005, sputum cultures still grew *M. tuberculosis*, and repeated DST showed resistance to HERS.

The patient was enrolled in a directly observed therapy program (DOT-plus) in 2007, and continued treatment with E, Z, Pto, Mfx, para-aminosalicylic acid, and rifabutin (Rfb). However, this sputum cultures remained positive. Despite the use of Group I–V antituberculosis drugs, the patient's sputum cultures remained positive at the time of this report. He was diagnosed to have chronic MDR-TB in 2009 and was placed in long-term isolation in a negative-pressure room.

2.2. Case 2

Case 2 is the third daughter of the index case. In 2002, she was diagnosed with pulmonary TB at the age of 19 years. At that time, the isolated strain was sensitive to HERS. She completed 8 months of treatment with HERZ and was cured in June 2003. However, in November 2006, a follow-up chest radiograph (Fig. 1B) and sputum cultures confirmed recurrent disease. DST showed resistance to HR, so she was treated with E, Z, S, Pto, and Mfx. Streptomycin was used for 6 months, and she completed an 18-month treatment course and was cured in September 2008.

2.3. Case 3

Case 3 is the index patient's older son. He was diagnosed with pulmonary TB in May 2005, at the age of 14 years, during a regular health checkup. A chest radiograph revealed infiltrations in the left upper lobe (Fig. 1C). He was treated with HERZS, but 2 months later DST showed HER resistance. The regimen was switched to Z, S, Pto, Rfb, and Mfx. Streptomycin was used for 7 months. He completed 18 months of treatment and was cured in January 2007.

2.4. Case 4

Case 4 is the index patient's younger son. He was first diagnosed in November 2006, at the age of 13 years. A chest radiograph revealed infiltrations and cavitations over the left upper lobe (Fig. 1D). The first *M. tuberculosis* isolate was fully drug susceptible, and he was treated with HERZ. However, due to persistent positive

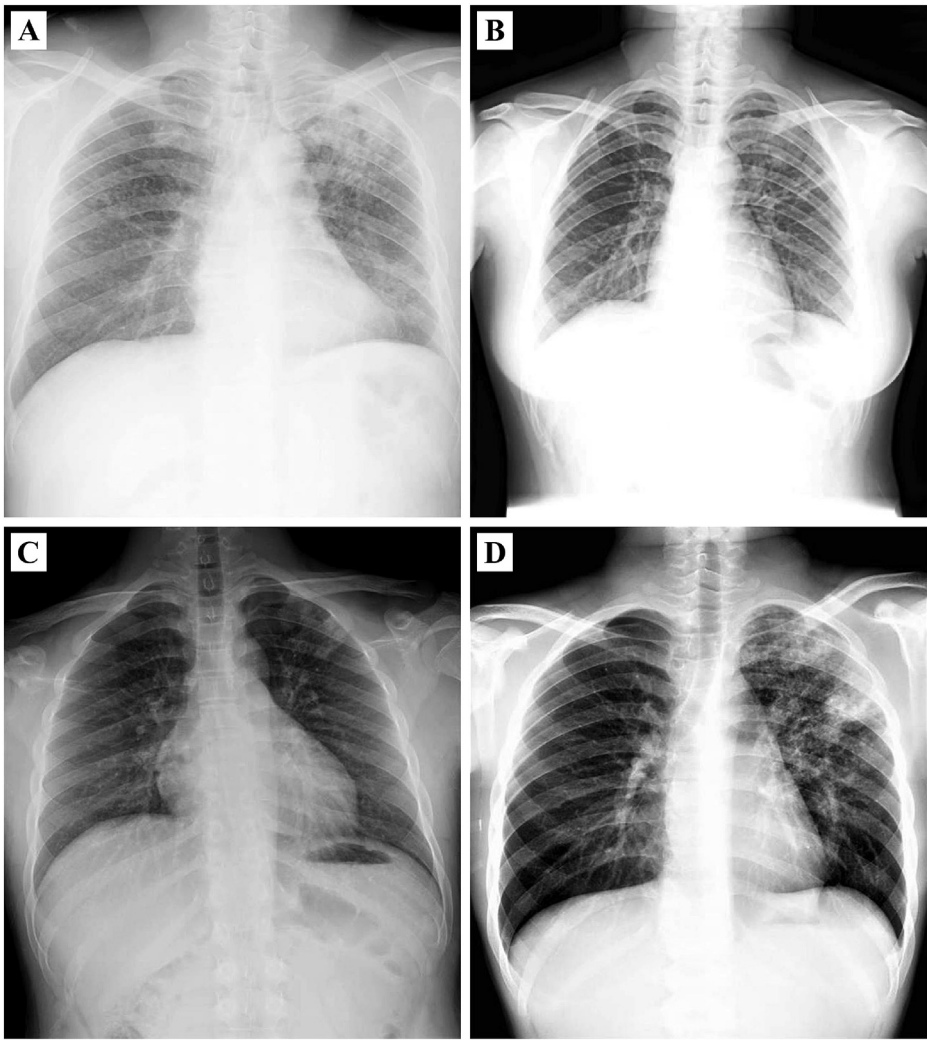

Fig. 1. Chest radiographs of four patients with multidrug-resistant tuberculosis: (A) Case 1, (B) Case 2, (C) Case 3, and (D) Case 4.