

A SUBSET OF CLINICAL STATUS OF PULMONARY TUBERCULOSIS IN SOUTHERN TAIWAN

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Abstract. The aims of this study were to present the clinical status of pulmonary tuberculosis in Southern Taiwan and to analyze the reasons for failure of antituberculosis treatment in order to achieve a higher rate of success after treatment. Two hundred and seventeen adult patients, aged 15 to 90 years old who presented to the Chest Division, Kaohsiung Medical University Hospital from 1999 to 2002 with a diagnosis of Pulmonary Tuberculosis, were retrospectively studied. We compared the rate of recurrence of pulmonary tuberculosis by dividing the cases into 2 groups: those who completed treatment and those who did not. We also determined the age distributions for when initial diagnosis of pulmonary tuberculosis was made among these 217 cases. In 90 culture proven cases, antituberculosis drug susceptibility was tested to determine the rate of drug resistance. We also assessed the reasons for failure of treatment. Age distribution analysis showed that initial infection began at a young age, was widely spread, and occurred regardless of age. There were 116 cases that completed antituberculosis treatment and 101 cases that did not. Of the 116 cases, only 16 relapsed, whereas 79 of the 101 cases relapsed. In cases where completely treated patients relapsed, the period before recurrence was indefinite. Most of the cases of incompletely treated patients relapsed earlier. In the 90 culture proven cases in which antituberculosis drug susceptibility was tested, 39 patients showed resistance to at least one drug, 9 patients were resistant to only one drug, 9 patients were resistant to two drugs and 21 patients were resistant to more than 3 drugs. The common reasons for failure of treatments were: 1) poor patient compliance to medication: 50 cases, 2) multiple drug resistance: 30 cases, 3) delayed treatment: 19 cases. Some cases included a combination of the above.

INTRODUCTION

The incidence of pulmonary tuberculosis has increased recently, although there were only about four thousand seven hundred cases of HIV (Human Immunodeficiency Virus) infection reported in Taiwan in the past 20 years. Studies were done on 217 cases of patients with present and/or previous pulmonary tuberculosis who had visited the Chest Division of Internal Medicine, Kaohsiung Medical University Hospital from 1999 to 2002. We tried to present the data of the current clinical status of pulmonary tuberculosis in this area and the recurrence rate of the infection, as well as to analyze antituberculosis drug resistance and the

reasons for failure of treatment in order to achieve a higher rate of treatment success.

MATERIALS AND METHODS

We retrospectively studied 217 cases of adult patients with present and/or previous pulmonary tuberculosis who had visited the Chest Division of Internal Medicine, Kaohsiung Medical University Hospital from 1999 to 2002. All of the cases were studied retrospectively. Pulmonary tuberculosis was diagnosed based on the following methods (Bates, 1979; Thomas, 1986; Weg, 1988; Catanzaro *et al*, 2000; Harries *et al*, 2001): (1) sputum, transbronchial washing or brushing fluid, or pleural effusion smear and/or culture was positive for tuberculosis bacilli. On the condition in which smear without culture was performed, the clinical course was consistent with pulmonary tuberculosis; (2) transbronchial or pleural biopsy revealed typical Langerhans giant cell granuloma

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with positive tuberculosis bacilli by acid-fast stain or culture; (3) clinical course, including clinical presentation, chest radiographs and empirical treatment, was consistent with pulmonary tuberculosis. The series of chest radiographs were reviewed by two national board certified radiologists and one national board certified pulmonary specialist; (4) patient's past medical history confirmed pulmonary tuberculosis which had been treated with antituberculosis medication and had been regularly followed at the clinic.

We compared the rate of recurrence of pulmonary tuberculosis by dividing the cases into 2 groups: those who completed treatment and those who did not. A complete course of treatment consisted of one of the following (MacGregor, 1988; Barnes and Barrows, 1993; American Thoracic Society, 1994; US Department of Health and Human Services Public Health Service, 1994a; Society of Internal Medicine of Taiwan, 1995; Ormerod, 2001): (1) ethambutol and isoniazid for at least 18 months or ethambutol, isoniazid and pyrazinamide for at least 9 months; (2) ethambutol and rifampin for at least 12 months or ethambutol, rifampin and pyrazinamide for at least 6 months; (3) isoniazid and rifampin (or plus ethambutol) for 9 months; or (4) isoniazid, rifampin, ethambutol and pyrazinamide for 6 months. Incompletely treated cases included poor patient compliance to medication, delayed treatment secondary to misdiagnosis, as well as some cases with irregular medication. In the culture proven 90 cases, we routinely performed drug susceptibility tests with isoniazid, ethambutol, pyrazinamide, rifampin, streptomycin, kanamycin and cycloserine to assess the patients' drug resistance. We also determined the age distribution for when initial diagnosis of pulmonary tuberculosis was made among these 217 cases. We also assessed the reasons for failure of treatment.

RESULTS

Age distribution analysis showed that initial infection began at a young age, was widely spread, and occurred regardless of age-with a predominance of cases among older individuals (Fig 1). There were 116 cases that completed antituberculosis treatment and 101 cases that did not.

Of the 116 cases, only 16 relapsed, whereas 79 of the 101 incompletely treated cases relapsed. The recurrence rate of incompletely treated patients (78.2%) was much higher than that of completely treated patients (13.8%) (Table 1). In cases where completely treated patients relapsed, the period before recurrence was indefinite (Fig 2). However, some cases were only followed up for a short period of time. Most of the cases of incompletely treated patients relapsed earlier (Fig 3.) The non-recurrent cases in the incompletely treated group were only followed for one to ten years. In the 90 culture proven cases in which antituberculosis drug susceptibility was tested, 39 patients (43%) showed resistance to at least one drug, 9 patients (10%) were resistant to only one drug, including 7 with primary resistance, 9 patients (10%) were resistant to two drugs, including 4 with primary resistance, and 21 patients (23%) were resistant to more than 3 drugs, including 6 with primary resistance. The common reasons for failure of treatments were: 1) poor patient compliance to medication: 50 cases; 2) multiple drug resistance: 30 cases; 3) delayed treatment: 19 cases. Some cases included a combination of the above.

DISCUSSION

In Kaohsiung, Bacille Calmette-Guerin (BCG) Vaccination (Menzies and Vissandjee, 1992) is routinely and widely performed for prophylaxis of tuberculosis in infant and children. Purified Protein Derivative (PPD) Skin Test is not popular for predicting infection in this area. Age

Table 1
Comparison of complete and incomplete antituberculosis treatment.

Classified antituberculosis treatment	Complete antituberculosis treatment	Incomplete antituberculosis treatment
Total cases (N)	116	101
Non-recurrent cases (N)	100	22
Recurrent cases (N)	16	79
Recurrence rate (%)	13.8	78.2

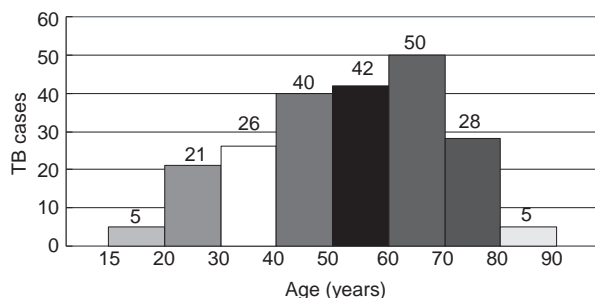


Fig 1—Age distribution of 217 cases of pulmonary tuberculosis.

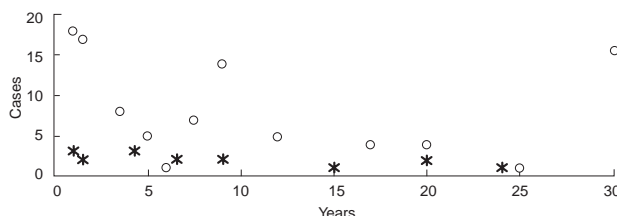


Fig 2—Clinical courses of complete antituberculous treatment (recurrent cases vs non-recurrent cases); ○ non-recurrent pulmonary tuberculosis cases; * recurrent and/or persistent pulmonary tuberculosis cases.

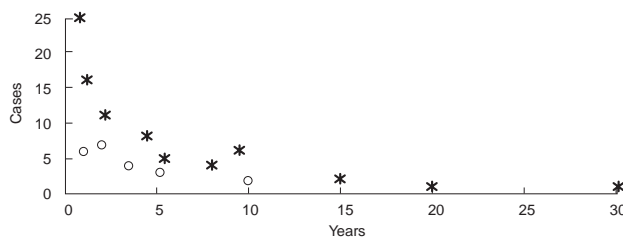


Fig 3—Clinical courses of incomplete antituberculous treatment (recurrent cases vs non-recurrent cases); ○ non-recurrent pulmonary tuberculosis cases; * recurrent and/or persistent pulmonary tuberculosis cases

distribution analysis showed that initial infection began at a young age, was widely spread, and occurred regardless of age. Because there were only about four thousand seven hundred cases of HIV infection in the past 20 years, the incidence of pulmonary tuberculosis brought on by HIV infection was not as high as that of other countries. Although the incidence of pulmonary tuberculosis is disproportional to tuberculous prophylaxis (US Department of Health and Human Services Public Health Service, 1990), preventive treat-

ment with BCG vaccination and/or antituberculosis drugs such as isoniazid or rifampin is strongly needed in this area. BCG vaccination has been routinely used as prophylaxis, but few people have had antituberculosis drug prophylaxis with a positive PPD skin test. The recurrence rate of incompletely treated patients (78.2%) was much higher than that of completed treated patients (13.8%). Even though the completely treated group had a lower rate of recurrence, it was still a disappointingly high ratio. It was difficult to distinguish between relapse and reinfection for those recurrent pulmonary tuberculosis cases. Relapse might take a short period of time to recur after treatment. Because there may be the same opportunity for reinfection, the incomplete treatment group could have a higher relapse rate and the complete treatment group a higher reinfection rate.

The completely treated patients had an unpredictable time of recurrence, which varied from the time of just finished antituberculosis medication to more than 20 years (Fig 2). Most of the non-recurrent cases of incompletely treated patients were only followed for a short period of time or for less than 10 years (Fig 3). If the non-recurrent cases were followed for longer periods of time, they might have a higher recurrence rate in the incompletely treated group. In the 90 culture proven cases where antituberculosis drug susceptibility was tested, 30 cases (33%) were resistant to at least two drugs and 21 of 30 cases (23%) resistant to more than 3 drugs, a high resistance rate. In order to achieve a higher rate of successful treatment, it is suggested that a drug susceptibility test be conducted routinely (American Thoracic Society, 1994; Michael and Iseman 1993).

Poor patient compliance to medication was a very common reason for failure of treatment. This can also induce a drug resistant strains of mycobacterium (Chawla *et al*, 1992; US Department of Health and Human Services Public Health Service, 1994a). The DOT method (Anonymous, 1993) (American Thoracic Society, 1994a; US

Department of Health and Human Services Public Health Service, 1994b) to achieve complete treatment is strongly needed in this area. It is dangerous to diagnose post-inflammatory fibrosis as an inactive lesion without antituberculosis treatment. Some lesions on chest radiographs might have remained constant for years before becoming active. Because of the high incidence and recurrence rates of pulmonary tuberculosis, the following is strongly suggested: (1) to lower the incidence of pulmonary tuberculosis, aggressive antituberculosis treatment is needed for active tuberculosis patients as well as prophylactic antituberculosis medication (Barnes and Barrons, 1993; American Thoracic Society, 1994) for patients with a positive PPD skin test and exposure to tuberculosis; (2) to achieve a higher rate of successful treatment, a drug susceptibility test should be conducted routinely due to the high rates of drug resistance; (3) the Directly Observed Therapy (DOT) method to achieve complete treatment is needed in this area due to poor medication compliance.

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