Tuberculosis in the CNMI: a case series

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Abstract

The incidence of TB in the Pacific people is among the highest worldwide. We analyzed the characteristics of 124 TB patients in the CNMI from 1989-93, none with HIV. The prevalence of TB during this period was 107 / 100,000. 79 patients had only PTB involvement; 25 had EXPTB tuberculosis; and 10 had combined PTB and EXPTB. Drug susceptibility data were available for 53 patients: 45 were pan-susceptible, 4 had resistance to SM, 3 to INH only and 1 to both INH and RIF, for total resistance rate of 15% (INH and SM resistance=7.5%, RIF resistance and MDR-TB= 2%). There were no differences in the susceptibility patterns of Micronesians and non-Micronesians. Radiological studies of 35 Micronesians were available. 13 had cavitary lesions, 11 showed intrathoracic adenopathy, 10 had alveolar infiltrates, 9pleural effusions, and 5 lower-zone TB. Two had a miliary pattern, and one patient had ARDS from TB. TB in Micronesia is characterized by high rates of extra pulmonary involvement, atypical chest radiographs, moderately low levels of primary drug resistance and MDR-TB and suboptimal compliance.

Introduction

Tuberculosis (TB) is a growing problem worldwide[1-3]. The combination of dual infection with the Human Immunodeficiency Virus (HIV)[4] and the emergence of multidrug-resistant tuberculosis[5,6] have led to the increase of TB cases in the USA and other countries[3,7]. Although Pacific people have high tuberculosis case rates[8-11], the usual clinical presentation of TB has not been described.

The CNMI consists of 14 islands with a surface area of around 470 square kilometers located in the western Pacific region. The current ethnic distribution of the population is quite mixed and many are workers from countries with high rates of TB. The Commonwealth Health Center (CHC) is the only hospital facility on Saipan and the seat of the public health administration. All TB patients in the CNMI are diagnosed and treated at this facility. Additionally, the CHC laboratory serves as the sole mycobacteriology laboratory for the CNMI. This study was undertaken to describe the demographic, clinical, bacteriological and radiological characteristics of TB patients in the CNMI.

Methods

Records of the TB clinic of CHC were reviewed for the years 1989 - 93. The charts of all patients with the diagnosis of active tuberculosis were reviewed. The diagnosis of active tuberculosis was made by a positive culture for Mycobacterium Tuberculosis, or based on clinical grounds (presence of symptoms, positive tuberculin test, compatible chest radiograph and response to therapy). The records of the microbiology laboratory were reviewed for mycobacterial smear and culture results. The date of diagnosis was defined as the date when the patient was started on therapy. Susceptibility testing was performed by an off-island reference laboratory using the critical concentration method. The radiographs were reviewed and characterized based on the absence or presence of cavitation, intrathoracic adenopathy, pleural effusions, alveolar-type infiltrates and the location of the abnormality. Atypical findings were defined as hilar or mediastinal adenopathy, miliary diseases, purely alveolar-type infiltrates, pleural effusions and infiltrates in the lower lung zones[13].

The intended duration of treatment was 9 months for those on isoniazid (INH) and rifampkin (RIF) only, and 6 months for the patients who had been treated with INH, RIF, pyrozinamide (PZA) with or without addition of a fourth drug, streptomycin (SM) or ethambutal (EMB). The actual duration of treatment was calculated as the time period between the date of diagnosis and the last day of therapy. To measure compliance, the actual duration of therapy was subtracted from the intended period (6 or 9 months based on the treatment protocol, see above). The patients who were repatriated were not included in the analysis of compliance. All patients were routinely questioned about HIV risk factors. A two-sided p value of less than 0.05 was considered statistically significant.

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Results

Demographics and clinical presentation: One hundred and twenty-four patients with tuberculosis were identified. Table 1 shows the ethnicity. All were newly diagnosed TB cases, and there were no relapses. The proportion of cases followed the overall ethnic composition of the CNMI as determined by the 1990 census. Accordingly, no ethnic group had a significantly higher ethnic-specific rate. The average case rate for the period of the study was 107 cases per 100,000, approximately 10 folds higher than the U.S. National average[14].

Table I. Demographic (N=124)	
Age (±SD)	32.4±13.0
M : F ratio	73:51
Ethnicity	No. (%)
Micronesia	47 (38%)
Filipino	59 (48%)
Chinese	12 (10%)
Korean	5 (4%)
Thai	1 (1%)

The age distribution of the Micronesians was similar to that of the non-Micronesians (35.4±18.6 vs. 30.6±11.9). Similarly, there were no differences in the gender distribution between the two groups (23 males and 24 females vs. 50 males and 27 females). Eighty-nine patients (72%) had only pulmonary involvement, 10 (8%) had combined pulmonary and extra pulmonary TB and 25 (20%) had only extra pulmonary involvement. The distribution of the extra pulmonary site of involvement is shown in Table 2. Micronesians and non-Micronesians had similar rates of extra pulmonary involvement (16/31 vs. 19/58). The patients with extra pulmonary TB were, on average, 8.2 years younger than those with pulmonary involvement (26.5±14.9 vs. 34.7±14.5, $p < 0.01$). This difference remained significant irrespective of ethnic background. Human Immunodeficiency Virus (HIV) serologic testing was routinely offered to TB patients in 1993 and was performed on 19. No patient showed HIV co-infection. Three other patients refused HIV testing. No patient had any known risk factors for HIV infection.

Table 2. Distribution of the extra pulmonary sites (N = 35)

Site	Number of patients (%)
Pleural	18 (51)
Lymphatic (extra and intrathoracic)	8 (23)
Miliary	4 (11)
Peritoneal	3 (9)
Other*	2 (6)

**One had tuberculosis of the parotid gland*

Bacteriology: Of the 99 patients with pulmonary involvement, 69 (70%) had sputum smear and/or culture positive for M. tuberculosis, and 30 (30%) were judged to have TB based on clinical grounds (chest radiographs, positive tuberculin skin tests, symptoms and response to therapy). Susceptibility testing results were available for 53 isolates. Of the 53, 45 (85%) were pan-susceptible. Of the remaining 8 isolates, 4 (7.5%) were resistant to SM only, and 4 (7.5%) were resistant to INH. Of the INH resistant isolates, 1 (2%) was also resistant to RIF. The overall rate of single drug resistance was 15%. There were no differences in the rate of drug resistance between Micronesians and non-Micronesians. Among the Filipino individuals, single drug resistance was noted in 2 out of 21 isolates (10%), and there were no MDR-TB cultures.

Therapy: Thirty-three of the patients left or were repatriated during the course of their therapy. These patients had similar rates of drug resistance and pulmonary involvement. One patient defaulted after approximately 4 months and refused to take any further therapy. Two patients with extra pulmonary TB refused treatment, and the rest (88 patients) completed the prescribed treatment protocol. The protocol prescribed by the attending physicians for 61 patients included therapy with INH, RIF and PZA for six months. For another 47 patients, SM or EMB was additionally prescribed. For the remaining 14 patients, the regimen prescribed consisted of only INH and RIF for 9 months. Overall, it took an additional 3.2±5.9 months (range 0 to 26) to complete the prescribed treatment protocol. It took an average of 11.7±7.8 months to treat the Micronesian TB patients, whereas, despite similar extent of disease, comparable treatment protocols and drug resistance, it only took 8.6±4.0 months to treat the non-Micronesians ($p<0.01$). Non-Micronesians had significantly better compliance than Micronesians (additional months required: 1.8±3.9 vs. 5.2±7.7, $p=0.01$, Figure 1). There were no deaths due to tuberculosis.

Radiological characteristics: Chest x-rays were available for 35 of the 47 Micronesians: 10 had infiltrates that were purely alveolar in quality, resembling a routine bacterial infection. Nine patients had pleural effusions, 11 had intrathoracic adenopathy (hilar and/or mediastinal), 13 had cavitary lesions-three in the basilar segments of the right or left lower lobes. Five patients had only lower zone infiltrates, two patients had miliary pattern and one patient had diffuse alveolar infiltrates. The latter patient developed adult respiratory distress syndrome (ARDS) due to tuberculosis and required prolonged mechanical ventilation. Overall, 20 patients (57%) had atypical chest x-rays. The distribution of the infiltrates was as follows: 12 patients, the infiltrates were located on the left, in 9 on the right and in 14 patients, bilateral involvement was noted.

Discussion

The Western Pacific region covers 35 countries spread over 19.9 million square kilometers. With a total population of 1.4 billion people and a high case rate, this region contains the largest number of TB patients in the world[9]. In the USA, Pacific people account for a disproportionately high number of TB cases[10]. Despite this high rate, there is very limited information on TB in Pacific people.

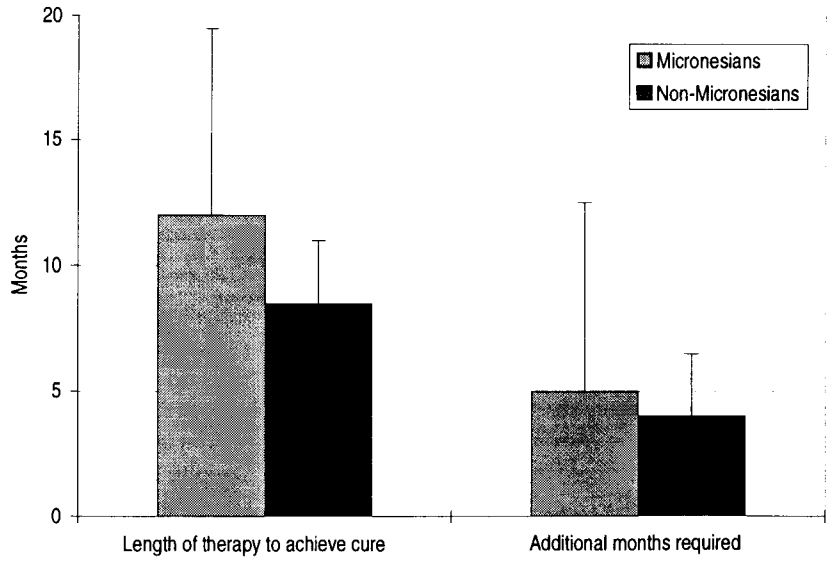
This study demonstrates that, despite the emergence of the new TB[15] in the USA and other countries, the dual epidemic of TB-HIV has not affected the CNMI. Only one patient with multidrug-resistant TB (resistant to, at least, INH and RIF). This patient had poor compliance with treatment and acquired drug resistance as a result. However, resistance to INH was seen in 7.5% of the isolates. Therefore, the therapy of TB in any Micronesian patient should include at least three drugs initially[16]. A surprising finding was the low rate of INH resistance and MDR-TB in individuals from countries with reports of high rates of drug resistance such as the Philippines[16,17]. In a study of Philippine World War II veterans immigrating to Hawaii, 12 out of 65 showed drug resistance, and 4/65 were multidrug-resistant (resistant to INH and rifampin). There were no MDR-TB isolates from Philippine nationals in this study and only one had INH resistance. The underlying reason for this difference is not clear. An explanation might be that the patients in this report were younger than the Hawaiian study and none had received any previous chemotherapy for TB. It is, therefore, plausible that our patients did not have the opportunity to develop drug resistance. An alternative explanation may be as follows: Although urban drug-resistant rates among patients with similar ethnic backgrounds have been reported to be high[18], many of the contract workers in the CNMI are originally from rural areas where the rate of drug-resistance may be lower.

Despite similar drug resistance and extent of disease, there was significantly better compliance with therapy among non-Micronesians. Many of these individuals are contract workers who reside in the CNMI on a temporary basis. Failure to report to the public health clinic results in institution of sanctions and, even, deportation. As a result of this investigation we have instituted incentive programs to further enhance the compliance of the indigenous population. These include food coupons after the completion of 3 and 6 months of therapy. The clinic is also initiating outreach work where the patient's medication is administered under direct observation at his or her place of work or residence. This is in an attempt to overcome potential problems such as lack of transportation and the need to take time off work.

Another finding of this study is the high rate of atypical chest radiographs seen in Micronesians. Although in the era of HIV infection atypical radiographic presentation is quite common[19], no patient in this report had dual HIV-TB infection. Prior to the AIDS epidemic, atypical findings had been reported in as many as one-third of the patients[13]. In this study, however, 20 out of 35 of patients had atypical findings. One might speculate that the high frequency of these atypical findings in this report as well as the high rate of extra pulmonary TB could represent a weaker immunologic status of Micronesians. Some experts believe that there are genetic differences in susceptibility to TB infection[20]. In the HIV infected TB patients, for example, it has been shown that lower immunity is associated with more frequent atypical chest radiographs and higher rates of EXPTB[21]. Another explanation could be that a substantial number of the CNMI TB cases are the result of recent infection, a phenomenon that has recently been described in the U.S.[22] Atypical findings are more common in chest radiographs from patients with primary and progressive primary TB[13]. Against this argument is the fact that our analysis failed to show any clustering of cases, and none of the patients had been institutionalized. The Chest Clinic Staff routinely perform contact investigation for each case of active TB, and this analysis did not show any clustering either. However, more sensitive methods, such as restriction fragment length polymorphism analysis, might have detected TB outbreaks with rapid progression to active disease during the study period[13].

Currently, the treatment of TB in the CNMI is entirely

Figure 1. Compliance with therapy was significantly better among non-Micronesians (p<=0.01 for both comparisons)



intermittent and directly observed. Universal adoption of directly observed therapy (DOT) has been advocated to improve compliance and decrease the risk of acquired drug resistance[24]. In a recent study, Weis *et al* showed that DOT for TB achieved significant reductions in the frequency of primary drug resistance, acquired drug resistance and relapse[25]. Although the prevalence of primary drug resistance in the CNMI is relatively low, by instituting DOT we hope to prevent the emergence of multidrug-resistant TB analogous to that seen in several large cities of the USA[5-7, 26].

In summary, TB in CNMI is characterized by high rates of extra pulmonary involvement, frequent atypical findings on the chest radiographs, absence of co-infection with HIV and low rates of drug resistance. However, given the proximity to and high degree of contact of Micronesians with countries with high HIV rates and drug-resistant TB[27], ongoing surveillance of drug susceptibility patterns and HIV serology is crucial.

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