STUDY OF TUBERCULOSIS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Abstract The research on tuberculosis (TB) comorbid with human immunodeficiency virus infections (HIV/TB), for which this prize was awarded, began with the author’s experience with Japan’s first HIV/TB case in 1992. In 1997, the clinical characteristics of six HIV/TB cases were presented in the Japanese Journal of Thoracic Diseases. In 2001, the author published a paper in Kekkaku on the anti-HIV antibody positive rate of TB patients. As part of a research team with the Japanese Ministry of Health, Labour and Welfare (2011–2013), the author surveyed the HIV/TB patients in the National Hospital Organization, and found a more or less unchanged mean 0.39% HIV-positive rate among TB patients. Among these TB cases, 2.1% were multidrug-resistant TB. In 2007, the results of Quantifier®-TB-2G (QFT-2G) HIV/TB analysis were reported in Kekkaku, showing the usefulness of QFT-2G in immunosuppression cases. Positive rates obtained with QFT-2G and Quantifier®-TB Gold (QFT-3G) declined when the peripheral blood lymphocyte count decreased, thought to be a result of QFT’s whole-blood collection methods. The author further studied the usefulness of interferon-gamma release assays (IGRAs) in HIV/TB with another health ministry research team (2009–2011). Enzyme-linked immunospot assay and QFT-3G were compared, which yielded better sensitivity and fewer indeterminate cases with the former. Periodic IGRAs were performed in IGRA-positive patients. Ten such cases (2 received isoniazid) were observed for more than 3 years, but none developed TB; however, IGRA values fluctuated during the observation period. It seems highly likely that immune function recovery through antiretroviral therapy lowered the risk of developing active TB. The author further examined the therapeutic interaction of rifampicin with anti-HIV drugs, confirming the feasibility of combining efavirenz and raltegravir. These results were presented at the annual meeting of the Japanese Society for Tuberculosis in Tokyo in 2012. The author intends to continue research with the hope of reducing HIV/TB incidence and improving prognosis.

Key words: Human immunodeficiency virus, Acquired immune deficiency syndrome, Tuberculosis, Interferon-gamma release assay, Multidrug-resistant tuberculosis, Efavirenz, Raltegravir

Introduction

The risk of developing active tuberculosis (TB) increases in many immunodeficient states but is highest in cases of human immunodeficiency (HIV) infection, which involve a marked decline in cellular immunity. Japan’s TB prevalence has declined to 16.1 cases per 100,000 people (2013); however, among other Western nations, prevalence is no more than five cases per 100,000 people, meaning TB is still moderately prevalent in Japan. The number of HIV/AIDS patients in Japan increased until 2008, eventually exceeding 1,500 new cases per year. Growth plateaued in 2009 but rose again in 2013 to the second-highest number of reported cases ever. In this environment, the number of comorbid HIV/TB cases appears unlikely to decrease.

The author treated Japan’s first case of HIV/TB at Tokyo National Hospital in 1992. By 1997, the author’s team reported a summary of six cases, and, to date, the author has experienced 85 HIV/TB cases. Since that initial case, the author has engaged in a variety of research on HIV/TB. The main findings are described below.

1. Surveying changes in HIV-positive rates among TB patients in Japan

The number of HIV/TB patients seen at Tokyo National Hospital has increased yearly since 1992. In most cases, an HIV test is performed if the TB is miliary or nonspecific, but some cases of classical pulmonary TB are found to be HIV-positive purely by chance. Thus, to examine the true extent of HIV-positivity among TB patients, we performed HIV tests on

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