Original Article

USEFULNESS OF T-SPOT®.*TB* IN THE DIAGNOSIS OF ACTIVE TUBERCULOSIS

Norio KODAKA, Kumiko KISHIMOTO, Takeshi OSHIO, and Hiroto MATSUSE

Abstract [Objectives] We investigated the usefulness of T-SPOT®.*TB*, an interferon-gamma release assay (IGRA), for diagnosis of active tuberculosis (*TB*) disease. We especially focused on the spot counts of T-SPOT®.*TB*.

[Methods] The present study included 92 patients who were suspected as pulmonary TB and showed positive results for T-SPOT®.*TB* between April 2013 and July 2015 at our department. These 92 patients were further divided into T-SPOT®.*TB* strong positive group (n＝35) and T-SPOT®.*TB* weak positive group (n＝57) based on the spot counts of T-SPOT®.*TB*. Clinical parameters were retrospectively analyzed.

[Results] *Mycobacterium tuberculosis* were determined by mycobacterial growth indicator tube (MGIT) culture in respiratory samples of 10 of 35 T-SPOT®.*TB* strong positive group and 7 of 57 T-SPOT®.*TB* weak positive group patients, indicating active TB was found significantly higher in the T-SPOT®.*TB* strong positive group (n＝35) compared to the T-SPOT®.*TB* weak positive group (n＝57) ($P<0.05$). In all T-SPOT®.*TB* positive patients, chest CT findings including cavity/small nodular/infiltration were found significantly higher in those with positive results for MGIT culture-confirmed tuberculosis than those with negative results for MGIT culture-confirmed tuberculosis ($P<0.05$).

[Conclusion] The present study indicates that the spot counts of T-SPOT®.*TB* is useful of supportive diagnostic methods for active TB disease.

Key words: Tuberculosis, Diagnosis, Interferon-gamma release assays, T-SPOT®.*TB*

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Original Article

STATUS AND PROBLEMS OF LATENT TUBERCULOSIS INFECTION IN THE UNIVERSITY OF THE RYUKYUS HOSPITAL

Shusaku HARANAGA, Momoko YAMAUCHI, Daijiro NABEYA, Kazuya MIYAGI, Masao TATEYAMA, and Jiro FUJITA

Abstract [Purpose] In 2011, the number of cases of latent tuberculosis infection (LTBI) in Japan reached its peak with 10,046 cases. In 2015, it decreased to 6,675 cases. Furthermore, the majority of LTBI cases have been described as patients with close contact to other tuberculosis patients; while, few have other risk factors. The present study aims to clarify the diagnosis and treatment outcomes of LTBI patients, in the University of the Ryukyus Hospital.

[Patient and Methods] Between January 2010 through December 2015, patients with LTBI were enrolled. Patient information including, clinical background, department reporting LTBI, immunosuppressive therapy, radiologic findings and treatment status were retrospectively collected from medical files and analyzed.

[Results] The annual number of LTBI patients increased sharply from 2012 to 2013 and gradually showed a decreasing. Overall, a total of ninety-two patients were diagnosed as LTBI. The department that most frequently diagnosed LTBI was the respiratory department, followed by nephrology, otolaryngology and gastroenterology department. In our cohort, solid cancer was the most common disease encountered in patients with LTBI. Renal disease and exposure to another TB patient were also common in LTBI patients.

In all cases, positive results of the interferon gamma release assay (IGRA) were confirmed. There were only four patients using biological products, five using immunosuppressive drugs, and thirty-one with high dose and long period steroid administration to treat underlying diseases. Seventy-two patients (80.9%) completed treatment for LTBI. In three cases, initial treatment with isoniazid was changed to rifampicin, due to drug related liver dysfunction.

[Discussion] At the University of Ryukyus Hospital, many cases of LTBI are diagnosed during routine hospital visits or following hospitalization due to basic diseases. This contrasts with the situation reported throughout the rest of Japan. Although LTBI was diagnosed in patients with solid malignancy frequently, few patients with diabetes were diagnosed. As such, it is presumed, LTBI may be underestimated in some patient groups (i.e., diabetes patients, dialysis patients or those using immunosuppressive therapy). Further insight into the nuances of LTBI diagnosis in patients with multiple and different underlying diseases is necessary.

Key words: Latent tuberculosis infection, University hospital, Immunosuppressive patients

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Case Report

A RETROSPECTIVE STUDY OF *MYCOBACTERIUM ABSCESSUS* COMPLEX PULMONARY DISEASES

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Abstract [Background] It is very difficult to treat *Mycobacterium abscessus* complex pulmonary disease (Mab-PD), the incidence of which is on the rise. This strain can be classified into three subspecies by a gene analysis, but few reports have described the clinical characteristics.

[Method] To elucidate the characteristics of Mab-PD, we retrospectively analyzed eight patients with Mab-PD in our hospital between January 2007 and December 2015. We examined the patients' characteristics, computed tomography (CT) findings, bacteriological examination findings, treatment and prognosis. To classify subspecies, the clinical specimens of three patients were analyzed by multiplex polymerase chain reaction (PCR) at the Department of Mycobacterium Reference and Research, the Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association.

[Results] The 8 patients comprised 5 males and 3 females with a mean age of 60.1 years (range 39−81). These eight patients suffered from the following underlying diseases: two cases of chronic obstructive pulmonary diseases, two cases of connective tissue diseases and one case each of concomitant malignant lymphoma and lung cancer, concomitant chronic progressive pulmonary aspergillosis and pleuroparenchymal fibroelastosis, bronchial asthma, and spino-cerebellar degeneration. One patient had been treated for *M.kansasii* in the past. Six of the eight patients had received multi-drug therapy, such as imipenem, clarithromycin, amikacin and others, for a mean of 19.2 months (range 7−35). Three patients who had continuously positive smear tests for acid-fast bacilli died despite treatment. We found two cases of *M.abscessus* subsp. *abscessus* and one case of *M.abscessus* subsp. *massiliense* by a classification analysis with multiplex PCR. Of the two cases of *M.abscessus* subsp. *abscessus*, one with progressive disease died due to multi-drug resistance. The patient with *M.abscessus* subsp. *massiliense* healed after 12 months of multi-drug therapy. No patients underwent surgical resection.

[Conclusion] These findings suggest that patients with Mab-PD need to have their subspecies identified due to their poor prognosis and the need for multi-modality therapy, such as multi-drug therapy and surgical resection. More cases should be accumulated, and new recommended therapies should be explored.

Key words: Nontuberculous mycobacteriosis, *Mycobacterium abscessus* subsp. *abscessus*, *Mycobacterium abscessus* subsp. *massiliense*, Multiplex PCR, Morphotype

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Field Activities

TUBERCULOSIS SURVEILLANCE SYSTEM IN TOKYO
— The Efforts of the Metropolitan Government and Its Achievements —

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Abstract Although the number of newly registered tuberculosis (TB) cases in Tokyo has steadily declined in recent years, incidence rates, TB patients' age distribution, their nationalities, and socio-economic conditions vary widely according to different areas across Tokyo. In addition, TB outbreaks occur in Tokyo several times every year, as well as the incidents of cases that require a large-scale contact investigation, often involving many public health centers.

In order to address such issues, the TB Epidemiology Center of the Tokyo Metropolitan Institute of Public Health (Center) launched a series of TB surveillance strengthening projects for better data collection and sharing information among public health centers in 2012. The projects include the routine systematic monitoring of newly registered TB patients, with special attention to TB cases such as infants, school children, and persons with special jobs, including school teachers, nursery staff, and nurses, who may expose other people around them on the job to infection. When such cases are identified in the database, the Center and the local public health center discuss necessary actions. Computer software was developed that assists public health centers analyzing TB problems in their service area. When the output of the TB Surveillance System is fed into this software, graphs are plotted showing trends of various parameters of the TB problem of the health center area, in comparison with those of the entire country and Tokyo.

A database of problematic cases of patients or incidents that have been discussed between public health centers and the Center is maintained. This database provides useful information as references for planning measures for similar new cases in the field.

Finally, we recently introduced a new computer TB Surveillance system that is accessible through an internet web site to assist collection and management of TB patient information, through cooperation of relevant institutions.

All these efforts of the Metropolitan government are expected to strengthen the TB control program activities of the public health centers in Tokyo.

Key words: Tuberculosis control, Epidemiology, Surveillance, Database, Public Health Center

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Review Article

ATTEMPTS TO FIND USEFUL NATURAL PRODUCT COMPOUNDS FOR ADJUNCTIVE CHEMOTHERAPY AGAINST REFRACTORY MYCOBACTERIOSIS

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Abstract Multidrug-resistant tuberculosis, or *Mycobacterium avium* complex infection, is a persistent disease characterized by the ineffectiveness of antimycobacterial drugs. The disease results in immuno-suppression and infection with dormant types of mycobacteria and, to date, available chemotherapy regimens are limited. Some natural product compounds, including Chinese herbal medicine and the extracts and derivatives of plants, have the potential to up-regulate host immunity, and are expected to have effects to complement conventional chemotherapy. The aim of this review was to investigate useful natural product compounds for adjunctive chemotherapy against refractory mycobacteriosis. We divided our discussion of the recent literature and our study into the following: first, clinical aspects of the efficacy of natural product compounds, including therapeutic values on long-term administration; second, immunological mechanisms associated with immunocompetent cells, cytokines, and transcription factors, revealing the potential biological activity of natural product compounds. Recent advances have resulted in a better understanding of refractory mycobacteriosis, promoted the investigation of modified regimens based on host immunity, and provided insight into the best use of natural product compounds for the development of therapies.

Key words: Mycobacterial infection, Tuberculosis, *Mycobacterium avium* complex, Herbal medicine, Traditional Chinese medicine, Chemotherapy

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