

CLINICAL UTILITY OF T-SPOT®.TB ASSAY WITH T-Cell *Xtend*® REAGENT FOR ACTIVE TUBERCULOSIS DIAGNOSIS IN THE FIELD TEST AT OUR HOSPITAL

¹Kenji NEMOTO, ¹Shuji OH-ISHI, ¹Masato TAGUCHI, ¹Kentaro HYODO,
¹Jun KANAZAWA, ¹Yukiko MIURA, ¹Takio TAKAKU, ²Shingo USUI,
¹Kenji HAYASHIHARA, and ¹Takefumi SAITO

Abstract [Background] T-SPOT.TB (T-SPOT), an interferon-gamma release assay, has shown promise as a diagnostic tool for active tuberculosis (TB), and its use is expanding. Addition of the T-Cell *Xtend* (TCX) reagent may allow delayed processing, and this characteristic is important for using this test in the field. However, limited data is available on the usefulness of T-SPOT with TCX as a field test for diagnosing active TB.

[Purpose] To investigate the clinical utility of T-SPOT with TCX and the risk factors for a false-negative result in patients with active TB.

[Methods] A total of 57 patients with active TB who underwent the T-SPOT test with TCX prior to treatment were enrolled between May 2013 and May 2015. One patient with an indeterminate result for T-SPOT was excluded; therefore, the data of 56 patients were eventually included in the final analysis. The basic characteristics and clinical findings were compared between the true-positive and false-negative T-SPOT groups.

[Results] Of the 56 patients, 40 (71.4%), 13 (23.2%), 3 (5.4%) had true-positive, false-negative, and borderline T-SPOT

results, respectively. This study did not reveal any significant risk factors for a false-negative T-SPOT result.

[Conclusion] In this clinical study, the proportion of patients with a false-negative result for T-SPOT with TCX for active TB was higher than that reported previously. Therefore, careful interpretation of a negative result for T-SPOT with TCX is necessary, regardless of the patient's background.

Key words : Active tuberculosis, False-negative, T-Cell *Xtend*, T-SPOT.TB

¹Department of Respiratory Medicine, ²Department of Thoracic Surgery, National Hospital Organization Ibarakihigashi National Hospital

Correspondence to: Kenji Nemoto, Department of Respiratory Medicine, National Hospital Organization Ibarakihigashi National Hospital, 825, Terunuma, Tokai-mura, Naka-gun, Ibaraki 319-1113 Japan.

(E-mail: nemoken1124@yahoo.co.jp)

AN OUTBREAK OF PULMONARY TUBERCULOSIS DUE TO DEFINITE EXOGENOUS REINFECTION AMONG ELDERLY INDIVIDUALS IN WELFARE FACILITIES

Shinichi IWAMOTO, Shuichi YANO, Emiko NISHIKAWA, Mitsuhiro TADA,
Toru KADOWAKI, Masahiro KIMURA, Kanako KOBAYASHI, and Toshikazu IKEDA

Abstract [Purpose] We report an outbreak of 64 cases of tuberculosis (TB) that spread in a welfare facility for elderly individuals.

[Objective and Methods] First, 64 TB patients who had contact with the source patient were screened at our hospital. We examined the time course up to the discovery of symptoms and analyzed the results for variable numbers of tandem repeats (VNTR) and the drug susceptibility tests. Second, we performed chest computed tomography to examine lesions due to a previous TB infection.

[Result] The source patient had recurrent aspiration pneumonia. The delay in doctor consultation was considered day 0, and the delay of diagnosis was 267 days. On examining the contacts, we found that 29 patients had TB while 35 had a latent TB infection. Results of the VNTR and the drug susceptibility tests showed that all the patients who developed TB had the same pattern as that of the source patient. Chest computed tomography showed lesions due to a previous TB

infection in 8 patients.

[Conclusion] Based on the results of the VNTR and drug susceptibility tests, we concluded that the outbreak was due to an exogenous infection from the same source. All 8 patients who showed lesions due to a previous TB infection were aged >81 years, and TB in these patients was found to be due to exogenous re-infection.

Key words: Exogenous reinfection, Mass outbreak, Variable numbers of tandem repeats, Drug susceptibility testing

Department of Pulmonary Medicine, National Hospital Organization Matsue Medical Center

Correspondence to: Shinichi Iwamoto, Department of Pulmonary Medicine, National Hospital Organization Matsue Medical Center, 5-8-31, Agenogi, Matsue-shi, Shimane 690-0015 Japan. (E-mail: shinichi.iwamoto@mmedc.jp)

Original Article

A SYSTEMATIC REVIEW ON THE PREVALENCE AND INCIDENCE OF
LATENT TUBERCULOSIS INFECTION AMONG PRISON POPULATION

Lisa KAWATSU, Kazuhiro UCHIMURA, Kiyohiko IZUMI, and Akihiro OHKADO

Abstract [Setting] We conducted a systematic review of literatures on the prevalence and incidence of latent tuberculosis infection in correctional settings, with the aim of offering one of the resources to guide establishment of policies on screening for and treating LTBI among prisoners in Japan.

[Objective] Using the keywords “latent tuberculosis AND (prison OR jail OR correctional)” and “tuberculosis infection AND (prison OR jail OR correctional)”, we conducted a systematic review of relevant literatures on PubMed and secondary searches from the reference list of primary sources. We limited our search to those original articles published since 1980, and in English.

[Results] 55 articles were identified, and 15 were subject to the systematic review. Of the 12 articles on prevalence of LTBI, 5 were from middle and high-burden and 7 from low-burden countries. The average prevalence of LTBI among middle and high-burden countries was 73.0%, and among low-burden countries, 40.3%. “Duration of incarceration” and “history of previous incarceration” were identified as risk factors for high LTBI prevalence which were specific to the prison population. Incidence of LTBI among the high-burden country was 61.8 per 100 person years, while 5.9 and 6.3 in

the two reports from low-burden countries.

[Conclusion] Prevalence and incidence of LTBI were higher than the general population, both in middle/high- and low-burden countries. The fact that “duration of incarceration” and “history of previous incarceration” were identified as risk factors indicate that high prevalence of LTBI among prison population is not just attributable to the characteristics of prisoners themselves, but also to the possibility of TB infection occurring in prison settings.

Key words: Tuberculosis, Incarcerated population, Latent tuberculosis infection (LTBI), Systematic review

Department of Epidemiology and Clinical Research, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association

Correspondence to: Lisa Kawatsu, Department of Epidemiology and Clinical Research, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-8533 Japan.
(E-mail: kawatsu@jata.or.jp)

Short Report

USE OF QuantiFERON®-TB Gold in Tube AND T-SPOT®.TB FOR DIAGNOSING PATIENTS WITH SUSPECTED PULMONARY TUBERCULOSIS

Niro OKIMOTO, Takeyuki KURIHARA, and Naoyuki MIYASHITA

Abstract [Objective] We analyzed the use of QFT®-TB Gold in Tube and T-SPOT®.TB in diagnosing patients with suspected pulmonary tuberculosis.

[Subjects and Methods] We evaluated 122 patients with suspected pulmonary tuberculosis (where chest X-ray showed consolidation or tumor shadow in predilection sites of pulmonary tuberculosis and through contact investigation). QFT®-TB Gold and T-SPOT®.TB were performed for all the patients. The positive response rate and history of pulmonary tuberculosis in patients who showed positive results for the tests were evaluated.

[Results] Nineteen patients showed positive results for QFT®-TB Gold, and 9, for T-SPOT®.TB. Four patients showed positive results for QFT®-TB Gold, and 3, for T-SPOT®.TB in 4 patients with active tuberculosis. The patients without active tuberculosis whose IGRAs were positive (old pulmonary tuberculosis, *Mycobacterium avium* complex, pneumonia, lung cancer, pulmonary sequestration, bronchiectasis) had a past

history of pulmonary tuberculosis.

[Conclusion] The positive result rate of QFT®-TB Gold was higher than that of T-SPOT®.TB in the subjects with suspected pulmonary tuberculosis. We think that QFT®-TB Gold reflected the past history of pulmonary tuberculosis.

Key words: Interferon-gamma release assay, QuantiFERON®-TB Gold in Tube, T-SPOT®.TB

Department of General Internal Medicine 1, Kawasaki Hospital, Kawasaki Medical School

Correspondence to: Niro Okimoto, Department of General Internal Medicine 1, Kawasaki Hospital, Kawasaki Medical School, 2-1-80, Nakasange, Kita-ku, Okayama-shi, Okayama 700-8505 Japan.

(E-mail: n.okimoto@med.kawasaki-m.ac.jp)

Short Report

MYCOBACTERIUM ABSCCESSUS PULMONARY DISEASE:
IMPORTANT PATHOGEN INVOLVED IN MICROBIAL SUBSTITUTION DURING
THE TREATMENT OF NON-ABSCCESSUS MYCOBACTERIAL DISEASE

¹Yoshiya TSUNODA, ¹Akimasa SEKINE, ¹Yuki SUMAZAKI, ¹Toru TANAKA,
¹Shih-Yuan LIN, ¹Hiroyuki TAKOI, ¹Kenji HAYASHIHARA,
²Ataru MORIYA, and ¹Takefumi SAITO

Abstract [Introduction] *Mycobacterium abscessus* pulmonary disease is common in patients with bronchiectasis. However, the underlying disease that is more likely to be present in patients with *M. abscessus* pulmonary disease remains poorly understood.

[Method] From 2001 through 2010, all patients, whose sputum or bronchoscopic lavage cultures yielded *M. abscessus*, were included in the study.

[Results] Among the 11 patients included (male/female: 4/7), 4 male patients had a history of smoking. All 11 patients presented with bronchiectasis on computed tomography before the detection of *M. abscessus*, and most patients demonstrated nodular bronchiectasis on chest computed tomography.

Six patients (54.5%) developed *M. abscessus* pulmonary disease during treatment for non-*abscessus* non-tuberculous mycobacterial disease: *M. avium* complex pulmonary disease in 5 and *M. kansasii* infection in 1. Although laboratory examination yielded negative findings for non-*abscessus* mycobacterium when *M. abscessus* was detected, radiographic deterioration was observed in 4 of 6 patients.

Five patients received drug therapy, 3 of whom were treated with multi-drug therapy including clarithromycin, ethambutol, and rifampicin, and the remaining 2 patients received low-dose macrolide therapy. However, *M. abscessus* was detected consistently in all patients, and deteriorated chest CT findings were

observed in 4. Among the remaining 6 patients untreated with drugs, sputum cultures yielded *M. abscessus* with radiographic deterioration in 4 patients.

[Conclusion] Our results indicated that *M. abscessus* infection developed during the treatment for non-*abscessus* mycobacterial disease, which was mainly due to *M. avium* complex pulmonary disease in most patients. *M. abscessus* infection thus occurred via microbial substitution. This phenomenon should be considered an important issue during the treatment for non-*abscessus* mycobacterial disease, which requires long-term medication.

Key words: *M. abscessus*, Underlying disease, MAC, Microbial substitution, Non-tuberculous mycobacteria

¹Department of Respiratory Medicine, ²Department of Clinical Laboratory, National Hospital Organization Ibarakihigashi National Hospital

Correspondence to: Yoshiya Tsunoda, Department of Respiratory Medicine, National Hospital Organization Ibarakihigashi National Hospital, 825, Terunuma, Tokai-mura, Nakagun, Ibaraki 319-1113 Japan.

(E-mail: chabo448@yahoo.co.jp)

Case Report

REACTIVATION OF TUBERCULOSIS PRESENTING WITH EMPYEMA
DUE TO ANTICANCER CHEMOTHERAPY FOR
DIFFUSE LARGE B CELL LYMPHOMA

¹Tatsuya YUBA, ²Mayumi HATSUSE, ³Mai KODAMA, ¹Sayaka UDA,
¹Akihiro YOSHIMURA, and ¹Naoko KURISU

Abstract A 79-year-old man with a history of tuberculosis was found to have chronic empyema in the right lung and was diagnosed with malignant diffuse large-cell lymphoma (Ann Arbor stage IIE). After completion of one course of rituximab plus cyclophosphamide, pirarubicin, vincristine, and prednisolone (R-CHOP) chemotherapy, the patient developed lung abscess and sepsis caused by *Streptococcus intermedius*. This condition was treated with antimicrobial agents, and chemotherapy was resumed. After the second course, the chemotherapy regimen was continued without prednisolone, and after administration of the third course, a chest wall mass was found in the right lung. An acid-fast bacillus smear test of the abscess aspirate was positive, and *Mycobacterium tuberculosis* was detected in a polymerase chain reaction assay, leading to a diagnosis of perithoracic tuberculosis. Chemotherapy for the lymphoma was discontinued, and treatment with four oral antitubercular agents was started. This treatment led to remission of perithoracic tuberculosis. In Japan,

tuberculous scar and chronic empyema are relatively common findings, and relapse of tuberculosis should always be considered for patients with these findings during chemotherapy and immunosuppressive therapy.

Key words: Malignant lymphoma, R-CHOP chemotherapy, Rituximab, Recurrence of tuberculosis

¹Departments of Respiratory Medicine, Kyoto First Red Cross Hospital, ²Internal Medicine, JCHO Kuramaguchi Medical Center, ³Department of Infectious Diseases, Kyoto Prefectural University of Medicine

Correspondence to: Tatsuya Yuba, Departments of Respiratory Medicine, Kyoto First Red Cross Hospital, 15-749 Honmachi, Higashiyama-ku, Kyoto-shi, Kyoto 605-0981 Japan.
(E-mail: tyb2001@gmail.com)

Report and Information

TUBERCULOSIS ANNUAL REPORT 2014**— (2) Tuberculosis in Pediatric and Elderly Patients —**

Tuberculosis Surveillance Center (TSC), RIT, JATA

Abstract In 2014, 49 pediatric tuberculosis (TB) patients aged 0–14 years were newly notified in Japan, with a notification rate of 0.30 per 100,000 population. Since 2006, the number of pediatric TB patients notified each year has been less than 100. Of the 49 patients, 17 (34.7%) were aged 0–4 years, 15 (30.6%) were 5–9 years, and 17 (34.7%) were 10–14 years. Until recently, the proportion of those aged 0–4 years was higher than those aged 10–14 years, but this year the proportions have become equal.

Of these 49, five had meningeal TB and two had miliary TB. In terms of case detection, 19 (38.8%) sought health care, while 25 (51.0%) were identified through contact investigations.

Since 2000, the number of all elderly patients (aged 65 years or older) with TB decreased rapidly, and remained stable until recently. However, the number of such patients has declined gradually since 2012. The proportion of TB patients aged 65 years or older has consistently increased to as high as 65.4% in 2014; notably, the proportion of TB patients aged 80 years or older has also increased to 37.7%. Since 1999, the TB notification rates in Japan have been consistently higher among patients aged 85 years or older than among those aged 65–84 years. The rate of notification for TB patients aged 65 years or older decreased by 3.1% from 2013 (13,227 patients) to 2014 (12,823 patients).

The proportion of bacteriologically positive TB patients among the general population of pulmonary TB (PTB) patients was higher among those aged 65 years or older than among those aged 15–64 years. Among all symptomatic patients,

the proportion of PTB patients with only non-respiratory symptoms increased with age to 28.5% among those aged 85 years or older. The proportion of TB patients with a patient delay of two months or longer was lower among patients aged 65 years or older than among those aged 15–64 years (14.5% vs. 28.2%), whereas the proportion of TB patients with a doctor delay of one month or longer was slightly higher among patients aged 65 years or older than among those aged 15–64 years (22.6% vs. 19.5%).

Among TB patients aged 65 years or older who were newly notified in 2013, 31.4% died within one year after the initiation of TB treatment; of these patients, 18.8% died within three months. The proportion of deaths within three months after the initiation of TB treatment increased substantially with age, from 8.8% of those aged 65–69 years to 35.6% of those aged 90 years or older.

Key words: Tuberculosis, Notification rate, Pediatric tuberculosis, Tuberculosis in the elderly, Annual trend

Research Institute of Tuberculosis (RIT), Japan Anti-Tuberculosis Association (JATA)

Correspondence to: Mayumi Suenaga, Department of Technical Assistance, RIT, JATA; Kazuhiro Uchimura, Department of Epidemiology and Clinical Research, RIT, JATA, 3-1-24, Matsuyama, Kiyose-shi, Tokyo 204-8533 Japan.
(E-mail: tbsur@jata.or.jp)