Original Article

INVESTIGATION OF A NEW TREATMENT OUTCOME INDEX FOR TUBERCULOSIS

Kunihiko ITO

Abstract [Purpose] To investigate a new treatment outcome index that may be useful in the Japanese tuberculosis surveillance system.

[Objective and Method] For sputum smear-positive primary tuberculosis patients, we estimated (a) treatment completion rates at the end of the next year of registration, and (b) treatment completion rates within 1 year from starting treatment in cases in which ≦1 year of treatment are indicated. For (a), we estimated treatment completion rates for newly registered cases during 2009 in the Japanese tuberculosis surveillance system, specifically at Fukujuji Hospital, which has a highly specialized tuberculosis treatment unit. For (b), we estimated the above-mentioned cases as well as those of "A" Public Health Center.

[Result] (a): The treatment completion rate at the end of the next year of registration was estimated to be 88.7% for newly registered cases during 2009 in the Japanese tuberculosis surveillance system. Among 66 jurisdictions, the highest and lowest completion rates were 100% and 58.3%, respectively, with a standard deviation of 6.7%. For Fukujuji Hospital cases, the completion rate was 93.1%. (b): The treatment completion rate within 1 year from the start of treatment was estimated to be 76.4% for newly registered cases during 2009 in the Japanese tuberculosis surveillance system. Among 66 jurisdictions, the highest and lowest completion rates were 90.9% and 44.1%, respectively, with a standard deviation of 8.8%. For Fukujuji Hospital and "A" Public Health Center cases, the completion rates were 91.1% and 80.0%, respectively.

[Conclusion] As a new treatment outcome index, treatment completion rates within 1 year might be more accurate than the treatment completion rate at the end of the next year of registration.

Key words: Lung tuberculosis, Sputum smear-positive, Treatment completion rate, Outcome index, Cohort analysis

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A CASE OF PULMONARY *MYCOBACTERIUM KANSASII* INFECTION WITH PLEURAL EFFUSION, DISTINGUISHED FROM PULMONARY TUBERCULOSIS

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Abstract A case of pulmonary *Mycobacterium kansasii* infection with pleural effusion is very rare. We report a case of pulmonary *Mycobacterium kansasii* infection with pleural effusion, distinguished from pulmonary tuberculosis. A 44-year-old man presented to a clinic with a productive cough, sputum, and loss of appetite for several months. Chest X-ray and chest computed tomography (CT) showed right pleural effusion, centrilobular nodules and infiltrative shadows with cavities in the bilateral lung fields. The direct smear examination showed positive acid-fast bacilli (Gaffky 5). He was referred to our hospital for suspected recurrent pulmonary tuberculosis. We started anti-tuberculosis drugs because pulmonary tuberculosis complicated with pleurisy was first suspected from the findings of high ADA level (78.6 IU/*l*) of the effusion and positive result of interferon-gamma release assay (QuantiFERON TB-2G). But *Mycobacterium tuberculosis* and *M.avium* complex was not identified by the polymerase chain reaction method and the culture of the sputum was negative. At a later date, *Mycobacterium kansasii* was detected by sputum culture. The patient was diagnosed as pulmonary *Mycobacterium kansasii* infection and treatment with anti-tuberculosis drugs including RFP resulted in a good clinical response. This case was a rare case of pulmonary *Mycobacterium kansasii* infection with pleural effusion, distinguished from pulmonary tuberculosis.

Key words: Pulmonary *Mycobacterium kansasii* infection, Pleural effusion, Pulmonary tuberculosis, Tuberculosis pleuritis, Nontuberculous mycobacteria

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THE EVALUATION OF THE UTILITY OF QuantiFERON®TB-GOLD IN-TUBE; QFT-GIT

Chairpersons: [1]Tomoshige MATSUMOTO and [2]ToshioYAMAZAKI

Abstract Four years has passed since QuantiFERON®TB-Gold In-Tube (QFT-GIT), the third generation test, has replaced QuantiFERON-Gold in Japan. The QFT-GIT test detects interferon-gamma (IFN-γ), which is released from lymphocytes present in blood after exposure to the *M.tuberculosis* complex antigens ESAT-6, CFP-10 and TB7.7. These proteins are absent from all Bacille-Calmette-Guérin (BCG) strains and from most non-tuberculosis mycobacteria, resulting in fewer false positive reactions as seen with the tuberculin skin test (TST). We had various experiences with QFT-GIT during these four years. So, we discussed the usefulness and its limitation of QFT-GIT as follows:

1. Development of the principle of QuantiFERON-GIT: Nobuyuki HARADA (Research Institute of Immune Diagnosis (RIID))

QuantiFERON (QFT) was originated from diagnostic system for bovine in Australia. Although the first generation of QFT, in which PPD had been used as stimulating antigens, was approved in USA, its diagnostic value was not recognized in Japan where most of Japanese are vaccinated with BCG. By combining *M.tuberculosis*-specific antigens with QFT system, the second generation of QFT, QFT-Gold, was developed, and approved in Japan in 2005. QFT-Gold was soon incorporated in several guidelines such as contact investigations and nosocomial infection measures. Now, QFT-Gold was superseded by the improved QFT-Gold, the current QFT-GIT. However, since QFT-GIT may contain unstable factors including blood volume and shaking methods of blood collection tubes, development of the more improved version is strongly expected.

2. Evaluating the result of QFT-GIT in patients treated with dialysis and immunosuppressive agents: Hidetoshi IGARI (National Hospital Organization Chiba-East National Hospital)

The effectiveness of QuantiFERON TB-Gold In-Tube was analyzed in the patients with chronic kidney disease (CKD) and rheumatoid arthritis (RA). QFT positive was 7% and 11% respectively, and indeterminate was 5% and 2% respectively. QFT positive was 2% in hemodialysis patients, significantly lower than that of CKD. QFT positive after biological drug was administered was 8% in RA patients, significantly lower than 15% of RA without biological drug. The rate of latent tuberculosis patients in CKD was as well as health care workers (HCWs) of 8% of QFT positive. On the other hand that of RA might be higher than HCWs. Hemodialysis and biological drug administration might attenuate QFT result with lower rate of positive. The rate of indeterminate was less than 5%. This results was improved in compared with former generation QFT.

3. QFT in Vietnam: Naoto KEICHO (Research Institute of Tuberculosis, JATA)

We have promoted collaborative research on tuberculosis with Vietnamese institutes since 2002. NCGM-BMH Medical Collaboration Center plays an important role in the clinical research projects. We report 1) quality assessment of QFT for tuberculosis infection, 2) prevalence and risk factors for tuberculosis infection among hospital workers, and 3) analysis of factors lowering sensitivity of QFT for active tuberculosis. We also discuss significance of QFT in developing countries.

4. Comparison of diagnostic performances using QFT Gold and Gold In-Tube in patients with active tuberculosis: Tetsuya YAGI (Department of Infectious Diseases, Center of National University Hospital for Infection Control, Nagoya University Hospital)

The goal of this study was to assess the diagnostic performances of QFT-GIT compared with QFT-Gold in patients with active tuberculosis in Nagoya University Hospital, in Japan. The sensitivity of QFT-Gold was 87.2%, the specificity of that was 77.5%. The sensitivity of QFT-GIT was 88.8%, specificity 73.2%. The performance of QFT-GIT was the same as that of QFT-Gold. The QFT-GIT tended to show higher concentration values of IFN-γ than that of QFT-Gold especially in patients with extra pulmonary tuberculosis, smear

positive pulmonary tuberculosis, both lung lesion and using immunosuppressive medications.

5. Simultaneous and longitudinal comparison between QFT Gold and Gold In-Tube among health care workers; Tomoshige MATSUMOTO (Department of Clinical Laboratory Medicine, Osaka Anti-Tuberculosis Association Osaka Hospital. ex-Osaka Prefectural Medical Center for Respiratory and Allergic Diseases)

The aim of this study was to compare the indeterminate rates between QFT-GIT and QFT-Gold tests. And to make longitudinal comparison by QFT-Gold assay to the same HCW. We collected blood samples by simultaneously QFT-Gold and QFT-GIT from 120 staff members in the institute who participated in this prospective comparison study. Moreover, the latest QFT-Gold test was longitudinally compared for the same 55 staff members who have received QFT-Gold before. The statistically significant difference was observed in the results of indeterminate rate between QFT-Gold and QFT-GIT using the same blood samples. It is concluded that QFT-Gold and QFT-GIT are different assays therefore it is difficult to compare QFT-Gold with QFT-GIT data on the same level. Concerning the follow-up test of the 55 people by QFT-Gold, 5 turned from positive to negative and 4 turned from indeterminate to negative. From this analysis, QFT-Gold positive subjects in the previous time have not been always positive.

6. Interpreting QFT "equivocal" results: Kenji MATSUMOTO (Osaka City Public Health Office)

The participants were examined QFT-GIT test after two months to four months from last contact of smear-positive tuberculosis cases in contact investigations. We enrolled 79 contacts whose tests of QFT-GIT were equivocal results. The second QFT-GIT results were 42 negative (53.2%), 28 equivocal (35.4%) and nine positive (11.4%). 64% of the second QFT-GIT tests result in negative or positive among the first QFT-GIT equivocal contacts. When the second QFT-GIT tests were positive, it is highly probable that the contacts were infected tuberculosis and we adequately could treat latent tuberculosis infected contacts.

Key words: QuantiFERON TB-Gold, QuantiFERON TB-Gold In-Tube

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