Original Article

OUTBREAK OF PULMONARY TUBERCULOSIS IN WHICH TUBERCULOSIS DEVELOPED FROM QuantiFERON®-TB SECOND GENERATION (QFT-2G) TEST NEGATIVE PERSONS

[1]Junichi YAMAGUCHI, [1]Yuko OOBA, [1]Mie KANEDA, [1]Kiyomi UCHIDA, [1]Yo ISHIKAWA, [2]Kiminori SUZUKI, [3]Takenori YAGI, [3]Yuka SASAKI, and [3]Fumio YAMAGISHI

Abstract [Purpose] To clarify the points to be considered when QFT-2G tests are used in the contacts examination by public health center.

[Object & Method] We analyzed the results of contacts examination on 43 workplace colleagues (39 y/o and younger) of a pulmonary tuberculosis patient (*b*Ⅱ2, Gaffky 9, cough for 1.5 months).

[Results] After two months of the last contact with the index case, tuberculin skin tests, QFT-2G tests and chest X-rays were undertaken. After 6 months, chest X-rays were taken, and after 9 months, QFT-2G tests and chest CT scans were also undertaken.

The tuberculin skin tests after two months showed a bimodal distribution, and 10 were QFT-2G positive and 2 showed doubtful reaction. The latter 12 persons underwent chemoprophylaxis. After 6 months, however, out of 31 QFT-2G negative persons, 2 developed pulmonary tuberculosis. Moreover, after 9 months, chest CT scans revealed 5 pulmonary tuberculosis patients. Three out of 7 new patients showed positive or doubtful reactions in QFT-2G tests undertaken after 9 months.

[Discussion and Conclusion] The sensitivity of QFT-2G tests is reported to be 80 to 90%, and the possibility of false negative is not negligible. We propose measures for public health center to conduct the contacts examination as follows; In case of high QFT-2G positive (including doubtful reaction) rate and/or a bimodal distribution of tuberculin skin test result, many infected persons are likely to be included in the group; and the following measures are recommended;

1) Necessity of chemoprophylaxis should be judged considering both tuberculin skin test results and the situation of contact with the index case, and not only by QFT-2G test results.

2) QFT-2G negative persons also need to be followed with chest X-rays.

Key words: QuantiFERON®-TB second generation (QFT-2G), Contacts examination, False negative, Chemoprophylaxis

[1]Public Health Office of Chiba City, [2]Chiba Foundation for Health Promotion & Disease Prevention, [3]National Hospital Organization Chiba-East National Hospital

Correspondence to: Junichi Yamaguchi, Department of Health Promotion, Public Health Office of Chiba City, 1−3−9, Saiwai-cho, Mihama-ku, Chiba-shi, Chiba 261−8755 Japan.
(E-mail: junichi-yamaguchi@city.chiba.jp)

Original Article

USEFULNESS OF A WHOLE BLOOD INTERFERON GAMMA ASSAY (QuantiFERON®-TB-2G) FOR DETECTING TUBERCULOSIS INFECTION IN HIV-INFECTED PERSONS

Hideaki NAGAI, Yoshiko KAWABE, Haruyuki ARIGA, Fumiko SHIGIYAMA, Masahiro SHIMADA, Makiko KUNOGI, Yoshinori MATSUI, Masahiro KAWASHIMA, Junko SUZUKI, Nobuharu OOSHIMA, Kimihiko MASUDA, Hirotoshi MATSUI, Atsuhisa TAMURA, Naohiro NAGAYAMA, Shinobu AKAGAWA, Kazuko MACHIDA, Atsuyuki KURASHIMA, and Hideki YOTSUMOTO

Abstract [Background] New blood test (QuantiFERON®-TB-2G: QFT-2G), based on detection of IFN-gamma released by T cells in response to *M. tuberculosis* specific antigens, has the high sensitivity and specificity for diagnosis of tuberculosis. However, it is essential to evaluate this T cell-based approach in individuals with HIV-associated impairment in T cell immunity.

[Methods] We assessed the usefulness of QFT-2G on diagnosis of tuberculosis in 13 HIV-infected patients with tuberculosis and the performance of 25 HIV infected persons under highly active antiretroviral treatment (HAART). QFT-2G, CD4 counts, and tuberculosis skin test and so on were examined.

[Results] The sensitivity of QFT-2G in HIV-infected patients with tuberculosis was 76.9%, which was significantly higher compared with tuberculin skin test, 15.4%. There was one indeterminate case of which CD4 count was 16/μl, the lowest count among the all patients. CD4 counts of 25 HIV infected persons under HAART were between 100 and 1157/μl. There were 3 QFT-2G positive cases among them, who had past history of tuberculosis.

[Conclusion] Although the very low CD4 counts in HIV-infected patients might adversely affect QFT-2G performance, the sensitivity of QFT-2G in the most of HIV-infected patients with tuberculosis was high, and it was thought that it was useful enough to diagnose tuberculosis infection. Careful observation is required in whether the recurrence of tuberculosis takes place among QFT-2G positive persons who have past history of tuberculosis.

Key words: Tuberculosis, HIV infection, QuantiFERON-TB-2G, ESAT-6, CFP-10

Department of Respiratory Diseases, National Hospital Organization Tokyo National Hospital

Correspondence to: Hideaki Nagai, Department of Respiratory Diseases, National Hospital Organization Tokyo National Hospital, 3−1−1, Takeoka, Kiyose-shi, Tokyo 204−8585 Japan. (E-mail: hnagai-in@tokyo-hosp.jp)

CLINICAL ANALYSIS OF DRUG INTERACTION BETWEEN RIFAMPICIN AND CLARITHROMYCIN WHICH ARE USED FOR TREATING PULMONARY *MYCOBACTERIUM AVIUM* COMPLEX INFECTION

[1]Hisashi TAKI, [2]Kenji OGAWA, [2]Taku NAKAGAWA, [2]Kaori KASHIMA, [2]Osamu TARUMI, [2]Yuko SAITOU, [2]Noritaka YAMADA, [2]Masao TANO and [3]Toshiaki NIKAI

Abstract [Purpose] We reviewed the interaction between rifampicin (RFP) and clarithromycin (CAM) during treatment of pulmonary *Mycobacterium avium* complex infection.

[Subjects and Methods] The subjects were patients with pulmonary non-tuberculous acid-fast bacillus infection during the period from September 2004 to January 2006 who consented to this study. Drug blood concentrations were compared with the minimum inhibitory concentrations for *M. avium* isolated from sputum and blood levels of CAM were assessed when the time of administration was changed for RFP.

[Results] The blood concentration of CAM showed a marked decrease in all cases (n＝6) when administered together with RFP, but there was no significant difference in the blood concentration of 14-R-hydroxy-clarithromycin (M-5), the active metabolite of CAM. However, the total blood concentration of CAM and M-5 showed a significant fall, similar to the blood concentration of CAM alone. When the blood concentration and bacterial MIC were compared for RFP, the blood concentration exceeded five MIC(s) in six samples as did the CAM＋M-5 level in four out of six samples. There was no significant difference in the blood concentration of CAM (n＝5) when the time of RFP administration was altered.

[Conclusion] Because the total blood concentration of CAM＋M-5 fell markedly by co-administration of RFP, this might have an influence on the antibacterial effect of CAM. In addition, examination of the administration of RFP and CAM at different times showed that the blood concentration of CAM did not increase and the influence of induction of hepatic drug-metabolizing enzymes by RFP could not be avoided.

Key words : Pulmonary *Mycobacterium avium* complex infection, Rifampicin, Clarithromycin, Drug interaction, Serum concentration, Minimum inhibitory concentrations

[1]Department of Pharmacy, [2]Department of Pulmonary Medicine, National Hospital Organization (NHO) Higashi Nagoya National Hospital, [3]Department of Microbiology, Faculty of Pharmacy, Meijo University

Correspondence to: Hisashi Taki, Department of Pharmacy, NHO Higashi Nagoya National Hospital, 5−101, Umemorizaka, Meito-ku, Nagoya-shi, Aichi 465−8620 Japan.
(E-mail: takih@toumei.hosp.go.jp)

Original Article

FEATURES OF BRONCHIAL TUBERCULOSIS
− An Analysis of 103 Cases −

[1]Atsuhisa TAMURA, [2]Akira HEBISAWA, [1]Kimihiko MASUDA, [1]Masahiro SHIMADA, [1]Makiko KUNOGI, [1]Yugo KANEKO, [1]Yoshinori MATSUI, [1]Masahiro KAWASHIMA, [1]Junko SUZUKI, [1]Haruyuki ARIGA, [1]Nobuharu OHSHIMA, [1]Hirotoshi MATSUI, [1]Hideaki NAGAI, [1]Shinobu AKAGAWA, [1]Naohiro NAGAYAMA, [1]Yoshiko KAWABE, [1]Kazuko MACHIDA, [1]Atsuyuki KURASHIMA, [1]Yutsuki NAKAJIMA, [1]Hideki YOTSUMOTO

Abstract [Objectives] The aim of this study is to clarify the features of bronchial tuberculosis.

[Materials and methods] We analyzed the clinicopathological data from 103 out of 4467 (2.3%) cases of culture positive tuberculosis admitted to the National Hospital Organization Tokyo National Hospital in the period from 1993 to 2004 in which bronchial tuberculosis was confirmed by bronchofiberscopy.

[Results] There were 62 women and 41 men, and 53 cases were less than 50 years old. The most common symptom, namely cough was observed in 70 cases, while 79 cases showed Ⅲ1 to Ⅲ2 on roentgenographic examination, and 81 cases were smear-positive for acid-fast bacilli in the sputum. Regarding the bronchofiberscopic findings, ulcers were detected in 60 cases, and the major site of bronchial tuberculosis was in the left main bronchus (35 cases). The number of the cases in which the time span from the onset of symptoms to diagnosis took over 3 months was 29, and 26 of them were "doctor's delay" cases which had a history of medical consultation resulting in diagnosis and treatment of other diseases, such as bronchial asthma (7 cases). There were 41 cases in which the second bronchofiberscopic findings have been reviewed, and regardless of the length of the span from the onset to diagnosis, the first bronchofiberscopy mostly revealed ulcer within 1 month after the start of treatment for tuberculosis, and 3 months after the start of treatment, many patients developed fibrous scars. Between 1999 to 2004, the first bronchofiberscopies were usually performed within 2 weeks to 1 month after the start of the treatment in contrast to the cases admitted between 1993 to 1998 in which bronchofribroscopy was mainly performed before the start of the treatment. However, there were no differences in the findings due to the timing of bronchofiberscopy.

[Conclusion] The clinical characteristics of bronchial tuberculosis have not changed, and the delay of diagnosis of bronchial tuberculosis due to doctor's delay also continues to be an important issue today. In patients showing positive sputum smear for mycobacteria, the timing of bronchofiberscopy, although required upon medical examination, is considered to be more appropriately performed from 2 weeks to 1 month after the start of treatment from the view point of nosocomial tuberculosis infection control strategy.

Key words: Bronchial tuberculosis, Bronchofiberscopic finding, Delay of diagnosis, Timing of bronchofiberscopy, Nosocomial tuberculosis infection control

[1]Department of Respiratory Diseases, and [2]Pathology, National Hospital Organization Tokyo National Hospital

Correspondence to: Atsuhisa Tamura, Department of Respiratory Diseases, National Hospital Organization Tokyo National Hospital, 3−1−1, Takeoka, Kiyose-shi, Tokyo 204−8585 Japan. (E-mail: tamura@tokyo.hosp.go.jp)

Short Report

TIMING OF QuantiFERON TB-G TEST FOR THE CONTACT EXAMINATION OF TUBERCULOSIS

[1, 2]Takashi YOSHIYAMA, [2]Nobuyuki HARADA, [2]Kazue HIGUCHI, and [1]Hideo OGATA

Abstract [Purpose] To investigate the timing when Quanti FERON®TB-Gold test (QFT-G) for the contact examination of tuberculosis should be done.

[Method] We examined QFT-G test for the 25 family contacts of sputum smear positive tuberculosis cases diagnosed at Fukujuji Hospital 5 times (soon after the diagnosis of the index case, 2 months later, 3 months later, 4 months later and 6 months later). And we calculated the positivity at these examinations.

[Results] Among 25 contacts, 8 persons became QFT-G positive. The positivity was higher among the contacts of cases with longer delay in diagnosis. 2 contacts were positive soon after the diagnosis of index cases, 5 cases became positive 2 months after the diagnosis and 1 case became positive after 3 months.

[Conclusion] 3 months interval from the diagnosis of the index case will be enough for the final decision of the infection of contacts.

Key words : Tuberculosis, QuantiFERON®TB-G, Contact examination

[1]Fukujuji Hospital, Japan Anti-Tuberculosis Association (JATA), [2]Research Institute of Tuberculosis, JATA

Correspondence to : Takashi Yoshiyama, Fukujuji Hospital, Japan Anti-Tuberculosis Association, 3−1−24, Matsuyama, Kiyose-shi, Tokyo 204−8522 Japan.
(E-mail : yoshiyama1962@yahoo.co.jp)