Original Article

LATENT TUBERCULOSIS INFECTION IN LUNG CANCER: A RETROSPECTIVE STUDY FROM A SINGLE CENTER

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Abstract [Objectives] The association between tuberculosis and lung cancer had drawn attention in terms of epidemiological and etiological connection, but the relationship between latent tuberculosis infection (LTBI) and lung cancer has rarely been discussed. To review the incidence and clinical characteristics of LTBI in lung cancer, we retrospectively studied lung cancer cases from a single center. [Methods] Clinical data of lung cancer diagnosed and treated at our hospital between 2004 and 2013, including interferon-gamma release assay (IGRA) results were analyzed. Patient groups included those with active tuberculosis (ATB), previous tuberculosis (PTB), LTBI, and non-LTBI. [Results] Of 1,518 lung cancer patients, 12 had ATB, and 61 had PTB. IGRA results were available for 511 of the remaining 1,445 patients, with 120 (23%) having LTBI and 341 non-LTBI. Multivariate analysis revealed that clinical features of LTBI patients were different from those of non-LTBI patients, including older age ($p<0.0001$; odds ratio [OR], 1.057; 95% confidence interval [CI], 1.030−1.086), a higher proportion of smokers ($p<0.0001$; OR, 3.429; 95% CI, 1.883−6.245), and a higher resection rate ($p=0.0024$; OR, 2.190; 95% CI, 1.320−3.634), whereas they were not significantly different from PTB patients, with the exception of a higher resection rate ($p=0.0032$; OR 2.948, 95% CI, 1.438−6.046). The overall survival of LTBI patients was similar to that of non-LTBI patients, but was better than that of PTB patients ($p=0.0146$; hazard ratio [HR], 1.608; 95% CI, 1.095−2.361). Three patients with PTB and none of the LTBI and/or non-LTBI patients developed active tuberculosis during a 5-year follow-up period, and the cumulative incidences ATB development among PTB patients were 1.74% (1 year), 4.31% (3 years), and 8.20% (5 years). [Conclusions] The rate of LTBI among patients with lung cancer in this study was 23%. The clinical status of LTBI was similar to that of PTB, but the prognosis was better. Risk of ATB development may be a consideration for PTB patients, but not for LTBI or non-LTBI patients.

Key words: Lung cancer, Interferon-gamma release assay, Latent tuberculosis infection, Previous tuberculosis

Original Article

SMOKING HABIT OF TUBERCULOSIS PATIENTS AND IT CHANGE DURING THE COURSE OF TREATMENT

Yuko YAMAUCHI, Yoko NAGATA, and Toru MORI

Abstract [Purposes] Smoking habits of tuberculosis (TB) patients aged 20 years or older were observed at the time of diagnosis and at the end of the treatment. These were newly registered at a total of 36 public health centers in 11 prefectures across Japan from 2010 through 2014.

[Results] At the time of diagnosis, the proportion of male smokers (smoking rate) was higher in all age groups in TB patients than in the general population; for females, it was higher in TB patients aged 40−59 years. The smoking rates of all ages of TB patients with age composition adjusted to that of the general population were 1.19 times higher for males and 1.23 times higher for females than those of the general population. Rate was also significantly higher among socio-economically disadvantaged patients that were defined as those receiving public welfare assistance and/or unemployed (aged less than 60 years). If the relative risk of TB among smokers is assumed to be 2.0, the population attributable fraction of smoking is estimated as 29% for males and 11% for females.

Among 378 patients who smoked at the time of diagnosis, 34.4% had stopped smoking (quitting rate), while 54.0% still smoked as before, and 11.6% continued smoking, though the amount of smoking was reduced, as reported upon completion of treatment. The quitting rate increased with age. The quitting rate was 33.8% for males, and 38.0% for females (difference not significant). The socio-economically disadvantaged patients had lower quitting rate of 26.4% compared with 36.3% for other patients, though the difference was not significant.

[Conclusions] When the harmful effects of smoking on tuberculosis have been proven clearly, it should be mandatory to address support of TB patients' quitting more strongly and effectively.

Key words: Tuberculosis, Smoking, Quitting, Patient support

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Original Article

THE STUDY OF IGRA FALSE NEGATIVE CASES IN THE PUBLIC HEALTH CENTERS IN KINKI AREA

Masahiro YAMADA and Takayuki MURAI

Abstract [Purpose] QFT-3G and T-SPOT tests are commonly used for contact investigations of tuberculosis at public health centers. It has been reported that positive rate of QFT-3G test tends to be higher than that of T-SPOT recently. So, IGRA false negative case study was performed with the purpose of accuracy control improvement of IGRA.

[Method] We researched for 3 years from 2014 to 2016 targeted for 64 public health centers in Kinki area by e-mail. This study included IGRA test results, IGRA false negative cases in contact investigations and newly notified tuberculosis cases.

[Results] The IGRA tests in contact investigations were in total 31,128 cases for 3 years, of which QFT-3G was 24,421 cases and T-SPOT was 6,707 cases. The IGRA false negative cases in contact investigations were 9 cases (0.03％) in total, of which QFT-3G was 3 cases (0.02％) and T-SPOT was 6 cases (0.10％), and the false negative rate of T-SPOT was significantly higher than that of QFT-3G ($p<0.01$). IGRA false negative cases in 7,648 cases of newly notified tuberculosis were 87 cases (1.1％) in total, of which QFT-3G was 19 cases and T-SPOT was 68 cases. In 96 cases with IGRA false negative results, of which 57 cases were pulmonary tuberculosis (59.4％) and 60 cases were extrapulmonary tuberculosis (62.5％) (Duplicate). The percentage of extrapulmonary tuberculosis in IGRA false negative cases was significantly higher than that of tuberculosis statistics in Japan in 2015 ($p<0.001$). There were 17 cases of diabetes (17.7％), 15 cases of cancer (15.6％), 8 cases of renal failure (8.3％) and 8 cases of steroid use (8.3％) in IGRA false negative cases.

[Discussion] We considered that it is important to diagnose tuberculosis carefully in cases with extrapulmonary tuberculosis and immunosuppressed conditions, even if IGRA result was negative.

Key words: Interferon-gamma release assay, QuantiFERON® TB Gold, T-SPOT®.*TB*, False negative, Contact investigation, Newly notified tuberculosis patient

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Original Article

THE AFFECTS OF NON-COMMUNICABLE DISEASES ON TREATMENT OUTCOME OF SMEAR POSITIVE PULMONARY TUBERCULOSIS

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Abstract [Objective] Japan is the top aging society in the world, and more than half of new notified TB were persons aged ≧70. Non-communicable diseases (NCDs) are also an increased risk for developing active tuberculosis. We collected the data asoociated with treatment outcome of new smear-positive pulmonary TB, and analyzed the effects of NCDs and aging on treatment outcome.

[Design] Retrospective cohort study. Subjects were patients admitted to Chiba-East National Hospital during 6 years from 2007−2012. Subjects were restricted to treatment naïve patients, and then total subjects were 618 [male/female＝438/180, average age＝60.1 yrs, range (12−99)]. Main outcomes were the ratio of treatment success and death.

[Results] The patients of age ≧70 was 219 (35％). There were 525 patients with some NCDs. The ratio of the patients with NCDs was 80.5％ in the group of age of less than 70, however, that was 93.2％ in the group of age of 70 or more, as was significantly higher. In a multivariate logistic analysis, independent predictors of treatment success included serum albumin ＜2.5 mg/dL (adjusted odds ratio 0.4, 95％ CI 0.2−0.7), cardiovascular disease (0.4, 0.2−0.96) and condition under immunosuppressive therapy (0.4, 0.2−0.9). And independent predictors of death included age (yr.) ≧70 (4.7, 2.3−9.7), serum albumin ＜2.5 mg/dL (3.1, 1.5−6.3), malignancy (8.7, 3.6−21) and cardiovascular disease (2.7, 1.1−6.6). Respiratory failure at admission, performance status (3 or 4) and standard regimen also affected the treatment outcome, and some NCDs were signicicantly associated with these three factors.

[Conclusion] NCDs and age (yr.) ≧70 was possibly associated with poor treatment outcomes in Japan. There are some countries with possible increase of the ratio of elderly population in the next 10 years, and elderly persons with NCDs might be another health theme for TB control program.

Key words: Non-communicable diseases, Aging, Pulmonary tuberculosis, Treatment outcome

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Case Report

TWO CASES OF PULMONARY *MYCOBACTERIUM SHINJUKUENSE* THAT REQUIRED THERAPEUTIC INTERVENTION DUE TO DISEASE PROGRESSION DURING TREATMENT-FREE FOLLOW-UP

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Abstract *Mycobacterium shinjukuense* is a nontuberculous mycobacteria that was first reported in Japan in 2011. However, the pathogenicity of this species and the treatment requirements for infection have not yet been established. We present two cases of pulmonary *Mycobacterium shinjukuense* infection that required therapeutic intervention due to disease progression during treatment-free follow-up.

The first case was that of a 62-year-old man. An acid-fast bacillus was identified from a bacterial culture of bronchial lavage fluid from the upper lobe of the right lung with bronchiectasis and nodular shadows. Although DNA-DNA hybridization (DDH) did not determine the bacterial species, *M. shinjukuense* was identified using gene sequencing. The second case was that of a 68-year-old woman. A chest CT examination showed a combination of bronchiectasis, nodular shadows, and consolidation in the lower lobe of the left lung. An acid-fast bacillus was identified using a bacterial culture of sputum and bronchial lavage fluid. Although DDH did not determine the bacterial species, *M. shinjukuense* was identified using gene sequencing.

In both cases, the patients' symptoms and chest radiograph findings worsened during treatment-free follow-up. Therefore, a therapeutic protocol for a pulmonary *M. avium* complex infection was initiated, and each patient improved. We considered that *M. shinjukuense* may be a pathogenic nontuberculous mycobacterial infection, although further clinical studies are necessary to clarify the optimal treatment regimen, therapeutic intervention may be required.

Key words: Pulmonary nontuberculous mycobacterial disease, *Mycobacterium shinjukuense*, DNA-DNA hybridization, Gene sequencing

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Case Report

A CASE OF ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS CAUSED BY RIFAMPICIN AND ETHAMBUTOL IN A PULMONARY TUBERCULOSIS

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Abstract We present the case of a 53-year-old female with pulmonary tuberculosis. She had psoriasis vulgaris and colon cancer. After admission, she was treated with four antitubercular agents: isoniazid (INH), rifampicin (RFP), ethambutol (EB), and pyrazinamide (PZA). However, 9 days after the treatment, she developed fever up to 38.5℃, erythema and pustules on the whole body. Therefore, we discontinued agents. Histological examination of skin biopsy revealed Kogoj's spongiform pustule and numerous neutrophils in the epidermis. After skin eruption disappeared, drugs were administered sequentially, and it became clear that the cause of skin eruption were RFP and EB.

Because the skin eruption and fever tended to disappear after the discontinuation of these drugs in one day and pathological findings showed Kogoj's spongiform pustule, we diagnosed acute generalized exanthematous pustulosis (AGEP), one of the drug-induced eruption. After that, we restarted INH and then added PZA, levofloxacin, and streptomycin sequentially, and the skin eruption didn't appear. We concluded that the continuation of treatment with the latter four drugs is possible, then she was discharged from the hospital. Development of AGEP due to antitubercular agents, such as INH and RFP, has been reported previously; however, reports on AGEP due to EB have not been observed. And reports on AGEP due to two antitubercular agents in one patient have not been observed. Thus, this case is rare. We should consider AGEP when we use antitubercular agents.

Key words: Pulmonary tuberculosis, Acute generalized exanthematous pustulosis (AGEP), Psoriasis vulgaris, Drug-induced eruption, Pustular psoriasis

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