Original Article

CLINICAL FEATURES ASSOCIATED WITH FALSE-NEGATIVE T-SPOT.*TB* ASSAY RESULTS IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Abstract [Background and Objective] Interferon-gamma release assays have demonstrated usefulness in the diagnosis of latent and active tuberculosis (TB). A meta-analysis has shown a sensitivity of 90% for T-SPOT.*TB*; this may be a potential problem in interpreting negative T-SPOT.*TB* results in patients suspected of having TB. We aimed to investigate the risk factors for false-negative T-SPOT.*TB* results in patients with pulmonary TB.

[Methods] A total of 237 patients with active pulmonary TB who underwent the T-SPOT.*TB* test prior to treatment were enrolled between January 2013 and August 2016. Patients with undetermined and intermediate results were excluded; therefore, 217 patients were included in the final analysis. Patients' characteristics, clinical laboratory findings and radiological findings were compared between the true-positive and false-negative T-SPOT.*TB* groups.

[Results] Of the 217 patients, 177 (81.6%) had true-positive and 40 (18.4%) had false-negative results. There were 135 men and 82 women, with a mean age of 68.1 years. On chest computed tomography scans, bilateral abnormal shadows were observed in 128 cases (59.0%) and cavity lesions were observed in 57 cases (26.3%). Multivariate analysis revealed that older age (≧80 years) [Odds ratio (OR) 0.44, 95% confidence interval (CI) 0.22−0.88, p=0.021] was an independent risk factor for false-negative T-SPOT.*TB* results.

[Conclusion] Careful interpretation of negative T-SPOT.*TB* results is necessary in elderly patients suspected of having pulmonary TB.

Key words: Pulmonary tuberculosis, Interferon-gamma release assays (IGRAs), T-SPOT, False-negative

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Original Article

THE SEASONALITY OF TUBERCULOSIS CASES WITH ENDOGENOUS REACTIVATION AMONG ELDELRY PERSONS, YAMAGATA PREFECTURE, JAPAN

Junji SETO and Tadayuki AHIKO

Abstract [Purpose] To clarify the periods associated with an increase of persons with tuberculosis (TB) onset and the periods needing attention for early TB diagnosis, we investigated the seasonality of TB cases with endogenous reactivation among elderly persons which make up the majority of TB cases in Japan.

[Methods] Among TB patients over 60 years of age in Yamagata Prefecture, Japan, during 2009−2015, we selected 296 persons as TB cases with endogenous reactivation of elderly persons who were judged to have less possibility of recent transmission by using molecular epidemiology for *Mycobacterium tuberculosis*. The case findings of the 296 cases were classified into six groups: 157 cases of outpatient visit with TB symptoms, 30 cases of emergency visit without TB symptoms, 26 cases of periodic outpatient with other diseases, 22 cases of medical checkup, 14 cases of TB non-specific symptoms in nursing home, and 47 cases of a miscellaneous group. The seasonality of TB cases in each group was analyzed by comparing between the highest and the lowest number of cases in three consecutive months. The seasonality of onset, first visit, and diagnosis were investigated in the group of outpatient visit with TB symptoms. For the other five groups, only seasonality of diagnosis was investigated. Wilcoxon rank-sum test was used for the analyses. We considered $P<0.05$ as statistically significant.

[Results] In the group of outpatient visit with TB symptoms, the number of the cases of TB onset in winter (December–February) was significantly ($P=0.021$) greater than that of in summer (June–August). Furthermore, the number of the cases of first visit in spring (March−May) was significantly ($P=0.017$) greater than that of in autumn (September–November). In the group of periodic outpatient with other diseases, the number of the cases of TB diagnosis during April–June was significantly ($P=0.023$) greater than that of during January−March.

[Discussion] Results suggest that the seasonality of TB cases exists in some case groupings among the cases of endogenous reactivation with elderly persons in Yamagata Prefecture, Japan. The seasons in which more cases of TB onset and first visit with TB symptoms appear (e.g., periods from winter to spring in outpatient visit with TB symptoms in this study) may be the optimal period for educational and awareness activities for driving early TB diagnosis in Japan.

Key words: Prevention of infection spread, *Mycobacterium tuberculosis*, Field epidemiology, Early detection, Variable-number tandem-repeat typing, Outpatient with tuberculosis symptoms

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Original Article

CLINICAL CHARACTERISTICS OF PULMONARY *MYCOBACTERIUM AVIUM* COMPLEX DISEASE WITH *PSEUDOMONAS AERUGINOSA*

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Akimasa SEKINE, Hideya KITAMURA, Tomohisa BABA, Shigeru KOMATSU,
and Takashi OGURA

Abstract [Objectives] Pulmonary *Mycobacterium avium* complex (MAC) disease is often complicated with co-infection of other microorganism. Although isolation of *Pseudomonas aeruginosa* is a poor prognostic factor of non-cystic bronchiectasis, few studies had reported about pulmonary MAC disease. In this study, we aimed to illustrate the clinical characteristics of pulmonary MAC disease with *P. aeruginosa* in comparison with those without *P. aeruginosa*.

[Patients and methods] We identified 322 patients with MAC disease who visited our hospital from April 2012 to March 2016. *P. aeruginosa* were isolated in 41 (12.7%) patients with pulmonary MAC, and clinical characteristics of MAC patients with *P. aeruginosa* were compared to those without *P. aeruginosa*.

[Results] Compared to MAC patients without *P.aeruginosa*, patients with *P.aeruginosa* had significantly lower body mass index (18.7 ± 2.9, $p < 0.05$), more affected lobes on CT scan ($p < 0.05$), and with concurrent isolation of other bacteria (68.3%, $p < 0.05$). Although not statistically significant, patients with *P.aeruginosa* tended to be older (71.3 ± 7.9), having lower lobe involvement on CT scan (86.5%), positive MAC antibody (82.6%), with concurrent isolation of other nontuberculous mycobacteria (14.6%), with higher resistant rate against clarithromycin (13.3%) and higher mortality (7.3%).

[Conclusion] MAC patients complicated with *P.aeruginosa* infection were more likely to have lower body mass index and more extended lesion, with no difference found on existence of cavity. Concurrent isolation of other bacteria including other nontuberculous mycobacteria was more often in those patients. A complication with *P.aeruginosa* infection in MAC disease may suggest a risk of co-infection with a variety of organism and poorer prognosis.

Key words: Nontubeculous mycobacteria, *Mycobacterium avium* complex, chronic *Pseudomonas aeruginosa* infection, *Mycobacterium avium* complex disease with *Pseudomonas aeruginosa*.

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Case Report

A CASE OF PULMONARY TUBERCULOSIS WITH NEGATIVE RESULT OF CAPILIA TB®, COMPLICATING LUNG ABSCESS WHICH PRESENTS DIFFICULTY IN DIAGNOSIS AND TREATMENT

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Abstract A 28-year-old male consulted our clinic for abnormal shadow in his chest X-ray and Chest plain CT, which showed nodular and granular shadows in the bilateral upper lung lobe. We found no evidence of mycobacterium organism by smear test from his sputum, gastric juice and bronchial lavage fluid, and couldn't find tuberculosis complex by PCR test from the same material. However the result of interferon gamma releasing assay was positive, so we started anti-tuberculosis therapy (HERZ). Before starting medication he complained of fever and we found a new infiltration shadow in the right lung field in his chest X-ray, and the shadow developed cavity formation after starting therapy. Four weeks after starting medication a mycobacterium culture test from bronchial lavage fluid proved positive but Capilia®TB-Neo (Capilia TB) was negative. Under diagnosis of lung abscess due to bacterium other than tuberculosis we stopped medication for tuberculosis and prescribed STFX, which resulted in improvement of symptom and laboratory data. However, the isolate from bronchial lavage fluid positive was identified *M.tuberculosis* complex by DNA-DNA hybridization (DDH) after seven days stopping the treatment with anti-tuberculosis agents. Therefore, the patient was diagnosed newly pulmonary TB disease, and received the TB treatment (HERZ) again. The clinical isolate with negative results by Capilia TB, which based on MPB64 protein detection has been developed for rapid identification of *M.tuberculosis* complex, and had mutations in the *mpb64* gene including a 63-bp deletion from nucleotides 196C to 258C. Capilia TB is a rapid and easy-to-use diagnostic kit detecting MPB64 protein, a specific secreting protein by tuberculosis complex, with high sensitivity and specificity. However we should keep in mind that there are rare false negative cases such as this case, and even if the result of Capilia TB is negative we must confirm by other methods such as genetic examination.

Key words: Pulmonary tuberculosis, Immunochromatographic assay, MPB 64 protein

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