Original Article

CONTACT INVESTIGATION USING QuantiFERON®-TB Gold TEST TO EVALUATE TB EXPOSURE IN 61 SUBJECTS IN A HOSPITAL SETTING

— (1) Outline of the Outbreak and its Clinical Picture —

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Abstract The index case was a patient who was admitted to a general hospital and treated with pulsed corticosteroid therapy; her breathing was assisted by a respirator. Soon she developed tuberculosis (TB) and died. Immediately after her death, QuantiFERON®-TB Gold (QFT) test was conducted in healthcare workers who were in close contact with the index case. From the results of the test, all the healthworkers except 1 were TB negative. However, the QFT test repeated in the healthworkers after 8 weeks was positive in 18.6%. Subsequently, 5 healthworkers, including a doctor, nurses, and radiology technicians, developed TB. Bacterial isolates from 3 of them showed restriction fragment length polymorphism (RFLP) patterns similar to that of the index case. These 3 secondary TB cases included one healthworker who was in contact with the index case for less than 5 min, another whose QFT was negative (or "doubtful" according to the Japanese criterion of the QFT), and a third who was TB positive for QFT test but declined treatment for latent TB infection (LTBI). No other healthworkers or hospitalized patients developed TB.

These healthcare workers with TB were further assessed using the QFT test at 6, 9, and 12 months after initial exposure, which showed an additional 4 positive reactors and 4 "doubtful" reactors who were indicated for LTBI treatment. Among these subjects, 7 were those who showed TB positive results 6 months after initial contact.

Discussions were made on TB prevention in hospital settings including contact investigations the staff with special reference to application of the QFT test.

Key words: TB exposure, QuantiFERON®-TB Gold (QFT) test, Contact investigations

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Original Article

EVALUATION OF GenoType® MTBDR*sl* FOR TESTING RESISTANCE OF *MYCOBACTERIUM TUBERCULOSIS* ISOLATES TO FLUOROQUINLONE, AMINOGLYCOSIDE, AND ETHAMBUTOL

Kinuyo CHIKAMATSU, Akio AONO, Hiroyuki YAMADA, and Satoshi MITARAI

Abstract [Objective] To evaluate the ability of GenoType® MTBDR*sl* (Hain Lifescience, Germany) in detecting resistance to fluoroquinolone (FQ), aminoglycoside (AG), and ethambutol (EB).

[Method] We evaluated the resistance of 76 *Mycobacterium tuberculosis* samples, namely, 13 extensively drug-resistant (XDR), 29 multi-drug resistant (MDR), and 4 susceptible clinical isolates from Japan, and 30 strains from Supra-national Reference Laboratory Network, to FQ, AG, and EB by using GenoType® MTBDR*sl*. The *gyrA*, *rrs*, and *embB* were directly sequenced for all the strains, and the mutations were confirmed. The susceptibility testing result obtained using the standard proportion method with 1% Ogawa medium was considered as the gold standard.

[Results] The sensitivities of GenoType® MTBDR*sl* for resistance to FQ, kanamycin (KM), amikacin (AMK), capreomycin (CPM), and EB were 82.4%, 57.1%, 100%, 83.3%, and 55.8%, respectively. The specificity for FQ was 97.6%, and that for KM, AMK, CPM, and EB were 100%. The mutant strains detected by GenoType® MTBDR*sl* were as follows: in 20 Japanese FQ resistant isolates, 7 *gyrA* MUT3A (D94A) (35.0%), 6 MUT3C (D94G) (30.0%), 2 MUT1 (A90V) (10.0%), and 1 MUT1 with MUT3C (5.0%); in 18 KM resistant isolates, 10 *rrs* MUT1 (A1401G) (55.6%); and in 34 EB resistant isolates, 9 *embB* MUT1B (M306V) (26.5%), 2 MUT1A (M306I) (5.9%), and 8 WT1 deficits (covering codon 306; 23.5%). Direct sequencing showed additional substitutions in *embB* (2 D328Y, 1 D354A, 1 G406D, and 1 G406S). The sensitivity of GenoType® MTBDR*sl* was similar to that by sequencing method for resistance to FQ and AG, but that for EB was slightly less than by sequencing method, but the difference was not significant.

[Discussion] The sensitivity of GenoType® MTBDR*sl* for the detection of FQ resistance was approximately 80% to that by standard drug sensitivity test results by using conventional proportion methods, while it was relatively less accurate for the diagnosis of resistance to KM and EB in Japanese isolates. Thus, GenoType® MTBDR*sl* is useful for the early diagnosis and infection control of XDR-TB, because of a short turn-around time of approximately 6 h.

Key words: Line Probe Assay, Fluoroquinolone, Aminoglycoside, Ethambutol, *gyrA*, *rrs*, *embB*, Multi-drug resistant *Mycobacterium tuberculosis*, Extensively drug-resistant *Mycobacterium tuberculosis*

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Original Article

CLINICAL ANALYSIS OF MYCOBACTERIOSIS PATIENTS WITH PNEUMOTHORAX

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Abstract [Background] Secondary pneumothorax caused by mycobacteriosis is rare. The frequency of incidence of pneumothorax in tuberculosis patients is reported to be only 1.5%, and that in nontuberculous mycobacteriosis patients may be very low. It is important to detect mycobacteriosis at an earlier stage in patients hospitalized for pneumothorax, in general wards so that nosocomial infections such as tuberculosis can be prevented.

[Objective] Chart review of mycobacteriosis patients with secondary pneumothorax admitted to the isolation ward, and that of the mycobacteriosis patients with pneumothorax admitted in the general wards of our hospital.

[Methods] We reviewed records of 555 mycobacteriosis patients admitted to the isolation ward of our hospital from January 2006 to December 2008. We analyzed the reasons for admission and cause, treatment, and outcome of pneumothorax.

[Results] Of the 555 mycobacteriosis patients, 11 (2.0%) had complications of pneumothorax. Among these 11 patients, 9 had tuberculosis, and 2 had nontuberculous mycobacteriosis. Of the 11, 5 were discharged, but 6 (54.5%) died during hospitalization, while among the remaining 544 mycobacteriosis patients without pneumothorax, 49 (9%) died during hospitalization. The hospital death rate of mycobacteriosis patients with pneumothorax was significantly higher than that of mycobacteriosis patients without pneumothorax ($p < 0.0001$). Among the 9 tuberculosis patients, 4 in whom pneumothorax was caused by rupturing of bullae showed improvement except one patient, but 5 in whom pneumothorax was caused by tuberculosis died.

Excluding the 555 patients admitted to the isolation ward, 388 pneumothorax patients were admitted to the general ward during the same period, among which 3 (0.8%) had mycobacteriosis.

[Conclusion] Tuberculosis-induced pneumothorax has a poor prognosis because the occurrence of tuberculosis impairs the mechanism of recovery from pneumothorax.

Key words: Nontuberculous mycobacteriosis, Tuberculosis, Pneumothorax, Secondary pneumothorax, Nosocomial infection

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Case Report

HEMOPTYSIS IN A PATIENT WITH OLD PULMONARY TUBERCULOSIS SHOWING ATYPICAL FINDINGS IN CHEST COMPUTED TOMOGRAPHY

Hiroaki SATOH, Katsunori KAGOHASHI, Gen OHARA, Kunihiko MIYAZAKI, Mio KAWAGUCHI, Koichi KURISHIMA, and Hiroichi ISHIKAWA

Abstract We report the case of an 85-year-old woman who had pulmonary tuberculosis when she was in her forties. She was referred to our hospital because of hemoptysis, which lasted for a few days. Her laboratory data was unremarkable. Chest computed tomography (CT) scan showed a thin-walled cavity with extensive calcification in the right S^2. There was no infiltrative shadow or bronchiectatic changes observed around the cavity. Active bleeding was observed to be occurring from the right B^2. After arterialization, embolization was performed in the right S^2. On the basis of the findings from this case, we recommend that clinicians perform bronchoscopy in patients with hemoptysis even if imaging studies show no typical findings suggesting hemorrhage. Further, although rare, old tuberculosis lesions such as a thin-walled cavity with calcification can cause hemoptysis.

Key words: Hemoptysis, Cavity, Calcification, Old pulmonary tuberculosis

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Case Report

CERVICAL LYMPHADENITIS CAUSED BY *MYCOBACTERIUM AVIUM* IN AN IMMUNOCOMPETENT ADULT

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Abstract Cervical lymphadenitis due to *Mycobacterium avium* complex is relatively common in children but is extremely rare in adults, except in immunocompromised patients. In this report, we describe a case of isolated cervical lymphadenitis in an immunocompetent adult woman. Histological examination of the excised lymph node showed multiple epithelioid cell granulomata with necrosis. Further, from the biopsy specimen cultures, we identified the causative organism as *Mycobacterium avium*. The patient was not administered any antimycobacterial agents because the affected lymph node was removed completely and because of uncertainty regarding the benefits of such treatment. No recurrence was observed in the patient's neck region during postoperative follow-up at 8 months.

Key words: *Mycobacterium avium*, Cervical lymphadenitis, Immunocompetent adult

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Case Report

ENLARGEMENT OF INTRATHORACIC DIFFUSE LARGE B-CELL LYMPHOMA DURING TREATMENT OF PULMONARY TUBERCULOSIS: A CASE REPORT

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Abstract We described enlargement of intrathoracic diffuse large B-cell lymphoma (DLBCL) during treatment of pulmonary tuberculosis in a 78-year-old man. The patient had previously undergone treatment for pulmonary tuberculosis about 50 years ago and showed disease recurrence in 2010. Although after tuberculosis treatment with the standard chemotherapy regimen of isoniazid, rifampicin, ethambutol, and pyrazinamide, we observed a clear resolution of the main X-ray shadows, a nodular shadow in the right upper lung field was observed to have increased in size. After evaluation by transbronchial biopsy of the upper right lung lobe, we diagnosed DLBCL with subepithelial infiltration of an airway. This is a rare case of coexistence of active pulmonary tuberculosis and intrathoracic DLBCL.

Key words: Diffuse large B-cell lymphoma (DLBCL), Pulmonary tuberculosis, Intrathoracic lymphoma, Lung cancer

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Tuberculosis Surveillance Center (TSC), RIT, JATA

Abstract We reviewed the tuberculosis (TB) surveillance database to determine the mode of detection, delays in achieving a TB diagnosis, and patients' occupational status upon registration.

Of the 23,261 TB patients who were newly notified in 2010, 81.7% were diagnosed at medical institutions. Of these, 12.0% were diagnosed during hospitalisation with a disease other than TB, and 9.9% were diagnosed during outpatient visits with diseases other than TB. The overall proportion of TB cases detected by contact examination was only 2.8%, but this mode of detection was higher (56.1%) among younger TB patients aged 0−14 years.

Of the 18,328 pulmonary TB patients, 27.3% had only respiratory symptoms, 31.0% had both respiratory and other symptoms, and 16.4% had only non-respiratory symptoms. Approximately one-quarter of elderly patients aged ≧ 80 years with symptomatic pulmonary TB had only non-respiratory symptoms.

Patients with positive sputum smears for symptomatic pulmonary TB tended to have long total delays (the amount of time between the onset of symptoms and diagnosis). Among elderly patients, patient delays tended to be short, whereas doctor delays tended to be long.

Of the 2,785 female pulmonary TB patients aged 20−59 years, 14.5% were medical workers and 10.4% of these were nurses.

Key words: Tuberculosis, Mode of detection, Delays in diagnosis, Occupation, Sex, Age

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