Current Topics

SURGICAL TREATMENT OF PULMONARY MYCOBACTERIOSIS FOR THE PAST 10 YEARS

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[1]Tetsushi SUITO, and [1]Shimao FUKAI

Abstract For the past 10 years (2000−2009), 50 patients of pulmonary mycobacteriosis underwent surgical treatment at Ibarakihigashi National Hospital. Three MDR-TB cases received lobectomy and one case of MDR-TB received intracavity aspiration and thoracoplasty. One bronchial tuberculosis received sleeve lobectomy. Two cases with hemoptysis due to *M.avium* pulmonary disease underwent pulmonary resection (lobectomy and completion pneumonectomy). One nontuberculous mycobacteriosis case accompanied by lung cancer received lobectomy. In one case because cavity lesion remained after chemotherapy she received lobectomy. All of patients were discharged without complication after operation.

For the purpose of definite diagnosis 41 cases (38 cases with a solitary pulmonary nodule and 3 cases with multiple pulmonary nodules) were received surgical procedures. Results of culture examination for the resected lesion were 4 *M.tuberculosis* complex, 8 *M.avium* and 4 *M.intracellulare*. There was only one case with *M.avium* who needed additional lobectomy because scattered lesions became worse after the previous pulmonary partial resection. The remaining patients were discharged without complication.

Key words: Pulmonary mycobacteriosis, Multi-drug resistant tuberculosis, Nontuberculous mycobacteriosis, Surgical treatment

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Current Topics

SURGERY FOR TUBERCULOSIS—A TEN-YEAR EXPERIENCE

Keisuke EGUCHI, Kohji KIKUCHI, and Mitsuo NAKAYAMA

Abstract We reviewed our institutional experience of surgical cases of tuberculosis in the last decade. There were 42 surgical cases, including 26 cases of tuberculoma, 5 cases of tuberculous lymphadenitis, 4 cases of tracheobronchial tuberculosis, and 7 cases of tuberculous empyema. The most aim of the surgery for tuberculoma and lymphadenitis were to make differential diagnosis from malignant neoplasm. Sleeve resection was done in 3 cases of tracheobronchial tuberculosis and Montgomery T-tube placement was underwent for a case of tracheal stenosis. Radical surgery was indicated for 4 cases of empyema and open window thoracostomy for 3 cases. There was no major complication and operation-related death. The surgical indication for tuberculosis is very limited nowadays because of effective chemotherapy, however, surgery is still relevant in selected small groups of tuberculosis patients. Exchanging more information and alliance among physicians and thoracic surgeons will become more important for better tuberculosis treatment.

Key words: Tuberculoma, Tuberculous lymphadenitis, Tracheobronchial tuberculosis, Tuberculous empyema, Surgery

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Current Topics

SURGICAL TREATMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS

Yuji SHIRAISHI

Abstract Although the results of medical treatment for multidrug-resistant tuberculosis (MDR-TB) has improved, adjuvant surgical treatment remains achieving better outcomes for MDR-TB patients. We have performed pulmonary resection for MDR-TB patients aggressively. Indications for surgery include (1) persistent positive sputum despite state-of-the-art chemotherapy and (2) a high risk of relapse. For 56 patients undergoing 61 pulmonary resections for MDR-TB between January 2000 and June 2007 at our institution, the overall cure rate was 98%. An aggressive treatment approach to MDR-TB continues to be justified until a panacea for this refractory disease is available.

Key words : Multidrug-resistant tuberculosis, Pulmonary resection, Operative morbidity

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Original Article

CHRONOLOGICAL CHANGE OF PRIMARY TYPE PULMONARY *MYCOBACTERIUM AVIUM-INTRACELLULARE* COMPLEX INFECTION

Hisayuki OSOREDA and Hideo KOBAYASHI

Abstract [Objectives] Primary pulmonary *Mycobacterium avium-intracellulare* complex (MAC) disease was evaluated from the viewpoint of chronological change.

[Method] From 1993 to March 2009, 130 patients with primary-type MAC disease were divided into three groups according to the period of time when they were diagnosed as below, and compared between groups by retrospective review.

[Results] Average numbers of cases per year were 5.12 patients in the 1st period (from 1993 to 2002), 10.98 in the 2nd period (from 2002 to 2006), 15.87 in the 3rd period (from 2006 to 2009). The number of cases per year gradually increased with time, while the percentage of females gradually decreased with time (84.1%, 74.4%, 69.8% for each period, $p<0.05$). Patient BMIs (body mass indexes) showed an upward trend while CRP (C-reactive protein) and ESR (erythrocyte sedimentation rate) showed downward trends though these changes were not significant.

[Conclusion] Though primary-type MAC disease typically affects mid-elderly and slender women, the authors demonstrated that it is increasing among male and non-slender females. Changes in the clinical features of primary-type MAC disease over time were also observed.

Key words: Nontuberculous mycobacterial infection, *Mycobacterium avium-intracellulare* complex, Primary type, Chronological change, Nodular-bronchiectatic disease

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Original Article

CLINICAL AND RADIOLOGICAL FEATURES OF TUBERCULOUS PNEUMONIA IN PATIENTS WITH EMPHYSEMA

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Abstract [Purpose] To elucidate the clinical and radiological features of tuberculous pneumonia in patients with pulmonary emphysema.

[Material and Method] Three emphysematous cases diagnosed with tuberculous pneumonia are clinically and radiologically reviewed.

[Result] Case l was a 62-year-old male with an infiltrate in the right upper lobe. A CT scan showed diffuse emphysema and a nonsegmental infiltrate without typical signs of bronchogenic spread. Sputum was negative for acid-fast bacilli. The infiltrate showed a nonsegmental spread unresponsive to antibiotics. *Mycobacterium tuberculosis* grew from a needle biopsy specimen five weeks after admission. The infiltrate disappeared with antituberculous treatment. Case 2 was an 82-year-old male, who presented with seven weeks of low-grade fever followed by high fever and lobar pneumonia in the right upper lobe. Sputum was positive for acid-fast bacilli on smear and tuberculosis PCR, leading to a diagnosis of tuberculous pneumonia. Case 3 was a 57-year-old male who had a history of dry cough lasting for one month. CT findings included a diffuse emphysematous change and a left upper lobe infiltrate, indistinguishable from bacterial pneumonia. His bronchoalveolar lavage was positive for tuberculosis PCR, which led to a diagnosis of tuberculous pneumonia.

[Conclusion] Tuberculous pneumonia in emphysematous patients can be nonsegmental, lacks bronchogenic spread, is indistinguishable from bacterial pneumonia, and clinically shows a poor inflammatory reaction, which is distinct from classical "caseous pneumonia."

Key words: Tuberculous pneumonia, Emphysema, COPD, HRCT

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NON-TUBERCULOUS MYCOBACTERIUM STRAINS THAT SHOW POSITIVE TEST FOR IDENTIFICATION KITS OF *M. TUBERCULOSIS* COMPLEX

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[5]Shigeo TSUCHIYA, [6]Tomotada IWAMOTO, [7]Kazue NAKANAGA,
[4]Keiji HAYAKAWA, and [3]Hajime SAITO

Abstract [Objectives] Saito et al. isolated novel mycobacterium strains from the sputum of 12 patients with pulmonary disease. They reported, that the strains were clearly different from *Mycobacterium tuberculosis* (TB) in cultural, biochemical and immunological properties, despite the high homology (99.1%) of the 16S rRNA gene sequence between the two. Recently, we isolated four strains having similar properties as the above strains among mycobacterial strains that were sent to the Research Institute of Tuberculosis for identification. We examined these isolates using commercial systems for identification of mycobacteria.

[Materials] Four strains of the unidentified mycobacteria were used in this study.

[Methods] Tests used in the study included cultural on solid media, biochemical characteristics, DNA sequence analyses of 16S rRNA and *rpoB* genes, TRC, COBAS AMPLICOR, COBAS TaqMan, MTD, DDH, Accu-Probe, Capilia TB, and a drug susceptibility tests.

[Results] After three weeks of culture, smooth and non-photochromogenic colonies were formed. The niacin accumulation test was negative. The homologies of DNA sequence between the new strains and *M. tuberculosis* for 16S rRNA and *rpoB* genes were 97.8% and 90.2%, respectively. The tests with TRC and MTD kits were positive, whereas the tests with AMPLICOR, TaqMan, Accu-Probe and Capilia TB kits were negative. The organism was not identified with the DDH system.

Key words: TRC, TRC Rapid M. TB, MTD, DDH

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Review Article

ARCHAEOLOGY OF TUBERCLE BACILLI AND TUBERCULOSIS

Kazuro IWAI, Shinji MAEDA, and Yoshirou MURASE

Abstract Accumulated information obtained in the 10 years since the clarification of the whole genome arrangement of tubercle bacilli has enabled us to presume a long history of tubercle bacilli from its first appearance on earth to the present epidemics in the world. It is presumed that tubercle bacilli appeared around 35,000 years ago through horizontal transfer mutation from a kind of environmental mycobacteria that could be tracked back 2,500,000 years, and expanded thereafter by 'bottleneck effects'. These mutated mycobacterial species adapted to humans, appearing in central Africa and then being carried to India-Oceanian and Middle East countries. The oldest human bone tuberculosis in a mummy of 9,000 years ago was found on the east coast of the Mediterranean Sea. Explosive transmission of tuberculosis was presumed to have progressed along with urbanized human life in the world-oldest Mesopotamian culture, followed by spreading to other areas, including East Asia, the Mediterranean region, Russia, and North Europe. The second epidemics, caused by a mutated Beijing family of the modern type, prevailed in central China and Southeast Asian countries, following the marked population growth in this area during the next 1,000 years. The majority of Beijing family strains isolated in Japan and Korea are, however, found to be of the ancient type, differing from the isolates from continental China, which are mainly of the modern type. The results of these studies may cast a new light on the understanding of tuberculosis epidemiology and also clinical medicine.

Key words: Tubercle bacilli, Gene mutation, Mummy bone tuberculosis, Phylogenesis, Genogeography

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The 84th Annual Meeting Symposium

NEW TECHNOLOGIES AND QUALITY ASSURANCE FOR THE DIAGNOSIS OF TUBERCULOSIS

Chairpersons: [1]Takeshi HIGUCHI and [2]Satoshi MITARAI

Abstract There are two clearly different directions for the diagnosis of tuberculosis. One is to detect *Mycobacterium tuberculosis* bacilli directly from clinical specimens, and the other is to detect the immunological responses indicating *M. tuberculosis* infection. The former is mostly effective to diagnose already developed tuberculosis as a disease using bacteriological techniques, while the latter is useful to diagnose the infection itself and tuberculosis with paucibacillary manifestation. It means that the bacteriological examinations contribute to detect active tuberculosis, and the immunological methods are useful to diagnose latent or sub-clinical tuberculosis infections, respectively.

It is critical to assure the quality of laboratory examination results from the viewpoint of evidence based medicine. The laboratory results directly affect the management of the case/suspect, thus the quality should be accurate. Recently the hospitals and clinical laboratories are keen to obtain the certificates from ISO and other accreditation programme like Japan council for quality health care. Therefore, this symposium aimed to discuss the quality assurance of laboratory diagnostics for tuberculosis, including new technologies.

At first, Dr Kazue Higuchi explained the methodology and some knacks for the quality assurance of QuantiFERON TB-2G (QFT 2G), which is an *ex-vivo/in-vitro* whole blood assay and now utilised widely in many clinical settings using. She provided many information to secure the quality of QFT-2G referring specimen collection, preservation, transportation and laboratory process. She also provided technical information of QuantiFERON Gold, which recently became available in the market.

Mr Yoshimi Higurashi discussed the quality assurance of mycobacterial culture based on the experience of obtaining ISO15189 in his laboratory, and explained in detail about the problems for quality assurance in Japan.

Prof. Mitsuaki Nagasawa explained the molecular microbiological methods, mainly on the nucleic acid amplification (NAA) methods. He laid stress on the clinical importance of NAA coming from its rapidity and high sensitivity, and emphasised the necessity of quality assurance for NAA.

Dr Satoshi Mitarai explained the data from the external quality assessment programme, which has been conducted by the Japanese Society for Tuberculosis for these several years, and emphasised the preferable effect of quality assurance activities. He also explained the importance of drug susceptibility testing for a good case management.

The symposium may provide comprehensive idea to understand the current and future strategy for the good and reliable laboratory performances.

1. Quality assurance of QuantiFERON®TB-2/3G: Kazue HIGUCHI (Immunology Division, Department of Mycobacterium Research and Reference, Research Institute of Tuberculosis)

Although the use of QuantiFERON®TB-2G (QFT-2G) is expanding rapidly, there were the discrepancies of QFT-2G results between two different laboratories using same subjects. Thus, it has been noticed that the quality assurance of QFT-2G is important. We have carried out the quality assurances of QFT-2G twice so far. Among participated laboratories, nearly half of them were not acceptable in two quality assurances. However, many of those who had not been acceptable in the first quality assurance became acceptable in the second quality assurance, indicating that the introduction of the quality assurance could improve the accuracy of test skills. In addition to test skills, there are several factors which affect the QFT-2G test results. These include the storage time and storage temperature after blood collection. Our results showed that storage of blood samples at room temperature is more important factor than the storage time after blood collection, indicating that blood samples should be kept at room temperature until culture. The new version of QFT-2G (QFT-3G), which is more convenient in the first step of QFT (i.e. blood culture), has been approved in Japan. Therefore, the quality assurance including QFT-3G would be necessary to obtain more accurate test results.

2. Quality control and assurance for mycobacterial culture: Yoshimi HIGURASHI (Department of Infection Control and Prevention, The University of Tokyo Hospital)

It is important that carry on quality control and assurance for mycobacterial culture which patient care and prevent to hospital associated infection. According to NCCLS M22-A3 commercially prepared culture media, as routine quality control by the clinical laboratory, culture media is monitored by an overall quality program that correlates test procedure with clinical information, monitor items and specimen quality. When commercially prepared media used, check abnormalities in appearance of media or not and confirm no contamination before inoculate. For improvement culture test result that should perform quality control and assurance involve reagents, media, maintenance of incubator and automatic incubator system.

4. Quality assurance of anti-tuberculosis drug susceptibility

testing: Satoshi MITARAI (Deputy Head, Department of Mycobacterium Reference and Research, Research Institute of Tuberculosis)

Quality assurance (QA) is the key to improve and maintain the quality of anti-tuberculosis drug susceptibility testing. As the components of QA, internal quality control (IQC), external quality assessment (EQA) and training will be considered. Each component has advantage and disadvantage, so that all components should be well combined and implemented with good programmatic management. In practice, IQC and panel testing (QA) are most feasible methods, and will require systematic implementation and evaluation. It will be preferable if QA is systematically implemented and the laboratory performance is improved through the activity.

Key words: QuantiFERON, ISO15189, Quality control, Quality assurance, External Quality Assessment

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Abstract The disease condition of the patient at the time of diagnosis of tuberculosis (TB) greatly influences subsequent TB treatment and prognosis. Here we report on the data of HIV infection, diabetes and drug susceptibility test results, which were added to the central TB surveillance database from 2007.

In the TB surveillance system, the item 'HIV' was classified into three codes, 'has HIV', 'does not have HIV' and 'unknown'. Although it was requested that 'has HIV' and 'does not have HIV' be coded based on HIV test results, this rule was not strictly followed in public health centers, and medical institutions usually give information to a public health center only in the case of HIV positive. Therefore, 'does not have HIV' cannot be assumed based on the test result. Hence, we show only the number of TB patients having HIV infection.

In 2007−2008, 124 TB patients newly notified were reported as having HIV. Of those, 110 (88.7%) were male and 14 (11.3%) were female, and 25 (20.2%) were foreigners. Although the ages of those having HIV were broadly distributed from the 20's to 70's, most patients were from 30 to 44 years old.

As to diabetes, 12.9% (3,192/24,760) of newly notified TB patients in 2008 were reported as having diabetes, and this proportion was higher among males (15.0%) than females (9.2%).

Susceptibility test results of 8,505 culture positive pulmonary TB patients were obtained through the system in 2007−2008, among which 98 (1.2%) were MDR TB. The proportion of MDR was different between new treatment and retreatment cases, 0.6% of new treatment and 6.5% of retreatment, respectively. The proportion of MDR was the highest among 20's in both males and females. More than half of MDR TB patients in 20's were foreigners.

Key words: Tuberculosis, Sex, Age, Foreigner, HIV, Diabetes, Susceptibility test, MDR

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