

Original Article

CLINICAL COMPARISON OF MALE AND FEMALE PATIENTS
WITH PULMONARY DISEASE CAUSED BY
MYCOBACTERIUM AVIUM COMPLEX (P-MAC)

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Abstract [Objectives] The objective of this study was to clarify clinical feature of Pulmonary *Mycobacterium avium* complex disease (P-MAC).

[Method] The present study was performed in 120 patients with P-MAC diagnosed during the period from January 2000 to March 2007. We divided P-MAC patients into four groups by the clinical disease type and gender, and retrospectively examined the clinical characteristics.

[Results] The subjects were 15 male (NB-M) and 71 female (NB-F) patients with nodular bronchiectatic disease (NB), and 24 male (FC-M) and 10 female (FC-F) patients with fibrocavitary disease (FC). The average age was lowest in the NB-F group (58.0 yrs), and highest in the FC-M group (65.8 yrs). There were 17 patients in the FC-M group and only two patients in the FC-F group with a history of smoking. The average body mass index (BMI) was 16.9, with the lowest value in the FC-F group. In the FC-M group, most of the patients had underlying pulmonary disease, whereas in the FC-F group, only four patients had underlying old pulmonary tuberculosis. The average anterior-posterior dimension was

75.2 mm, being lowest in the FC-F group, and more than 90 mm in the other groups. The proportion of refractory cases was lowest in the NB-M group.

[Conclusion] We thought that we were able to clarify characteristics of patients with disease caused by MAC by analyzing the types of the disease separately in men and women.

Key words : Pulmonary *Mycobacterium avium* complex (MAC), Gender, Clinical feature

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MICROBIOLOGICAL PROPERTIES OF *M. PORCINUM* ISOLATED FROM A PATIENT WITH IMPAIRMENTS IN IL-12/IFN- γ PATHWAY

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and ²Hitoshi KAMIYA

Abstract [Purpose] *Mycobacterium porcinum* has been successfully isolated from the patient with abnormal signal transduction pathway of IL12/IFN- γ . The properties of each bacterium were determined by conventional identification methods, DNA sequencing analysis and MIC assay.

[Materials and Methods] *M. porcinum* was isolated 7 times from 1996 to 2007 from cervical lymph node, axillary lymph nodes, inguinal lymph node, brachial lymph node and site of a tumor of the patient. In another occasion, mycobacteria were isolated from lavage fluid of the endoscope in routine inspection. Using these mycobacteria, *M. porcinum* (ATCC33776) and *M. fortuitum* (ATCC6841), the conventional identification method and MIC assay were carried out. For analyses of the DNA sequencing (*rpoB*, *dnaJ* and *hsp65*), the ATCC type strain of mycobacteria (11 strains) which are closely related to *M. porcinum* were also used.

[Results and Discussion] DNA sequencing analyses of the 7 samples isolated from the patient, were concurrently identical in 3 different genes. Drug susceptibility test showed that 7 isolates had no marked change. In conventional identification analyses, *M. porcinum* (ATCC33776), *M. fortuitum*

(ATCC6841), and *M. porcinum* that were isolated in 1996, were able to grow at 42°C. However, 6 isolates that were isolated after 1999, did not grow at 42°C. The colony detectable days of these 7 strains changed from 3 to 7. Over the time, the morphology of each colony changed from smooth to rough. Though the initial isolate had the ability to utilize mannitol, the later 4 isolates had no such ability.

Key words: *Mycobacterium porcinum*, *M. fortuitum*, IL-12/IFN- γ pathway, Mendelian susceptibility to mycobacterial disease

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ACHIEVEMENT OF SPUTUM CULTURE NEGATIVE CONVERSION BY MINOCYCLINE IN A CASE WITH EXTENSIVELY DRUG-RESISTANT PULMONARY TUBERCULOSIS

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Abstract A 33-year male was readmitted to our hospital for the treatment of multi-drug resistant pulmonary tuberculosis in February 1993. Six years after the treatment, the left pleuro-pneumectomy was done because of the enlargement of cavitory lesions with formation of fluid. Four years after the operation, *M. tuberculosis* from the patient was resistant to all first- and second-line anti-tuberculosis drugs. Apical lesion and cavitory lesion on the upper lung were still seen on chest X ray and sputum smear and culture were continuously positive. Minocycline and gatifloxacin were prescribed after five years of the operation. Sixteen months after changing the regimen sputum smear and culture converted negative. Chemotherapy was terminated in August 2007, two years after the negative conversion. One year after the termination of treatment no relapse occurred. We considered minocycline

was effective in this case, because gatifloxacin was resistant by the drug susceptibility test and was previously used.

Key words: Extensively drug-resistant pulmonary tuberculosis, Minocycline, Surgical resection

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FOR PROPOSAL OF GUIDELINES FOR MANAGEMENT OF
EXTRA-PULMONARY TUBERCULOSIS
— Focused on Tuberculous Superficial Lymphadenitis and Pleural Tuberculosis —

Chairperson: Kunihiko ITO

Abstract: In clinical practice of lung tuberculosis, there are many data and evidence, and very useful guidelines are readily available. But in extra-pulmonary tuberculosis, we have limited data to guide our daily clinical practice, and therefore there are no definite guidelines. Probably there might be considerable variables in the clinical diagnosis and management of extra-pulmonary tuberculosis even among hospitals and/or doctors that have good experience in those types of tuberculosis. Under those situations, un-experienced clinicians might have difficulties to decide what is the best clinical practice to manage extra-pulmonary cases. Therefore proposal of some guidelines about the management of, at least, frequently encountered types of extra-pulmonary tuberculosis will be very useful to clinicians.

This symposium was focused on tuberculous superficial lymphadenitis and pleural tuberculosis, and the guidelines for diagnosis and treatment in both types of extra-pulmonary tuberculosis were proposed by four doctors who have considerable experience in those diseases. Many participants came

to this symposium, and very active discussions were held. This means, again, that many clinicians want some guidelines for management of extra-pulmonary tuberculosis.

This symposium was very short one, and the proposed guidelines in this symposium are, in fact, just the personal opinions. But we hope that in the near future, The Japanese Society for Tuberculosis will have more extensive symposiums about the management of extra-pulmonary tuberculosis and issue the official guidelines. This symposium is just the beginning of those processes.

1. Proposal of Diagnostic Guideline for Superficial Tuberculous Lymphadenitis : Literature Review and Our Experience. Takayuki NAGAI (Osaka Prefectural Hospital Organization Osaka Prefectural Medical Center for Respiratory and Allergic Diseases)

Diagnosis of superficial tuberculous lymphadenitis should be considered from various factors such as past history, palpation findings, image findings, AFB-smear and culture, TB-

PCR, cytology and histological findings. Using QFT (Quantiferon-TB-2G), that is regarded as a subordinate diagnosis, might be controversial. However, taking into consideration the fact that the positive rate of QFT is less than 5% among healthy people under 40 years old, and the incidence rate of malignant disease becomes higher over 50 years age, we show the algorithm of the diagnostic process for superficial tuberculosis lymphadenitis in Fig. If the patients are suspected to have tuberculous lymphadenitis, they should have fine needle aspiration for examine AFB-smear and culture, TB-PCR, cytology. If all the results are negative, the patients under 40 years old should be examined QFT test. The patients over 40 years old with positive reaction in QFT test should be suspected to have tuberculous lymphadenitis and be considered to have the diagnostic therapy. However, if the patients are over 40 years old or the patients under 40 years old have negative reaction in QFT test, they should have biopsy.

2. Treatment of cervical tuberculous lymphadenitis: Naoya KATSURAGI, Yuji SHIRAIISHI, Hidefumi KITA (Section of Chest Surgery, Fukujiji Hospital)

We studied 27 patients (32 cases) diagnosed with cervical tuberculous lymphadenitis, who were treated with chemotherapy in addition to surgery between January 1997 and September 2007. Enlarged lymph nodes were fluctuant and drained spontaneously with fistula formation in 15 patients, while 9 patients had erythema on the neck. Surgical procedures included incision and drainage of lymph nodes in 22 cases and lymph node excision in 10 cases. Most patients received chemotherapy with a 6- to 9-month regimen. One of the 27 patients relapsed 3 years after lymph node excision and underwent additional drainage. The cure rate was approximately 96% with a median follow-up of 41 months. A combined treatment of chemotherapy and surgery for cervical tuberculous lymphadenitis was shown to be useful in relieving the symptoms as well as for shortening the duration of treatment.

3. Guideline for the diagnosis of tuberculous pleurisy: Makoto MIKI (Department of Respiratory Medicine, Japanese Red Cross Sendai Hospital)

We encounter tuberculous pleurisies most among the extra-pulmonary tuberculosis in the clinical setting and the guideline is expected all over the world. Therefore I want to propose the following diagnostic criteria for a great deal of

discussion.

It is necessary for diagnosing that the pleural effusion is recognized on the chest radiograph or the computed tomography and the tubercle bacilli is directly proved with the specimen from thoracic cavity such as pleural effusion and pleura by using bacterial, biochemical and molecular biological methods. Thoracoscope is a powerful tool for the additional examination.

When the definite diagnosis is difficult, we should examine the bacterial test of sputum and gastric juice, the pathology of the pleural biopsy specimen and the adenosine deaminase (ADA) of the pleural effusion, exclude the exudative pleuritis of other causes, and decide the possible diagnosis comprehensively.

4. Treatment of tuberculous pleurisy: Kimihiko MASUDA (Department of Respiratory Disease, National Hospital Organization Tokyo National Hospital)

Tuberculous pleurisy is classified into two forms; namely, pleurisy with and without pulmonary tuberculosis. Fundamental treatment is anti-tuberculosis chemotherapy, however, the role of early drainage to avoid residual pleural thickening (RPT) remains unclear. Fifty-five patients with tuberculous pleurisy in these 5 years were reviewed in Tokyo National Hospital. Although early pleural drainage did not lower the incidence rate of RPT in pleurisy patients with pulmonary lesions (drainage: non-drainage = 3/9 : 0/7, $p > 0.05$), it lowered the incidence rate of RPT in pleurisy patients without pulmonary lesions (drainage : non-drainage = 0/23 : 4/16, $p < 0.05$). It is concluded that early pleural drainage may be effective to prevent occurrence of RPT in tuberculous pleurisy patients without pulmonary lesions.

Key words : Tuberculous lymphadenitis, Tuberculous pleurisy, Extra-pulmonary tuberculosis, Guideline

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————— The 83rd Annual Meeting Mini-symposium —————

TREATMENT MODALITY OF LATENT TUBERCULOSIS INFECTION

Chairperson: Kiminori SUZUKI

Abstract: In order to eradicate TB, LTBI should be a primary target in clinical practice. LTBI was reviewed and discussed from the standpoint of its historical perspectives, its current status in Japan, clinical problems of pediatric LTBI, and also from its practical treatment in future.

1. A history and clinical significance of treatment of latent tuberculosis infection: Kiminori SUZUKI (Chiba Foundation for Health Promotion and Disease Prevention)

The incidence ratio of TB in Japan shows a gradual decrease in recent years. In order to eradicate TB a primary target should be set toward its new infection and clinical outbreak. Treatment of LTBI is effective way to prevent clinical manifestation of the disease, and clinical survey of subjects who had an infectious contact with TB patients should be carried out on a clinical basis. A newly introduced diagnostic tool, QFT-2G, is to be effectively utilized for detection of LTBI and is considered to play an important role for LTBI control strategy.

2. Latent tuberculosis infection in Japan: Yuka SASAKI (Department of Thoracic Disease, National Hospital Organization Chiba-East National Hospital)

The Japanese Society for Tuberculosis (JST) revealed the statement for latent tuberculosis infection treatment in 2004, but in some of clinical environment the statement was not fully appreciated. We surveyed the status of latent tuberculosis infection in Japan by means of hospital-based questionnaires. A few of hemodialysis facilities take care of latent tuberculosis infection before induction of hemodialysis. The treatment of latent tuberculosis infection involves some points to be solved. Although the chest CT scan is one of ways to rule out active pulmonary tuberculosis, but it is not evaluated effectively. Latent tuberculosis infection should be tried to be detected and be treated actively.

3. Diagnosis and treatment of latent tuberculosis infection in children: Osamu TOKUNAGA, Takeshi MIYANOMAE

(Department of Pediatrics, National Hospital Organization Minami-Kyoto National Hospital)

Both early detection and treatment of LTBI in children are very important not only for the prevention of progression to active TB disease, but also for the future global TB elimination. Some problems on the diagnosis and treatment of LTBI in children remain unresolved: (1) usefulness of the QFT results in judging TB infection, (2) radiographic application to rule out active TB disease, (3) definition of the high risk children who should be screened for LTBI, and (4) optimal treatment regimen with excellent efficacy and good adherence. We reviewed the current consensus on the performance of QFT in diagnosing LTBI and the radiographic studies to rule out children with active TB.

4. Practical use and several disputable points in the guidelines of contact investigation for latent tuberculosis infection: Chika SHIRAI (Department of Health and Welfare of Hyogo ward of Kobe city)

Subjects itemized for discussion are as follows: (1) diagnosis of confirmed LTBI is difficult by plain chest X-ray examination, (2) report and registration of LTBI are not popular rule for clinical doctors, (3) adverse effects in treatment of LTBI for elderly people are not clear, (4) adherence of medication for LTBI is a burden to asymptomatic contact case, and (5) preventive DOTS for LTBI is necessary for control of MDR-TB.

Key words: Latent tuberculosis infection, Diagnosis, Treatment, Tuberculosis in children, Contact examination

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