

EVALUATION OF TUBERCULOSIS TRANSMISSION ROUTES IN AN OUTBREAK AMONG YOUNG ADULTS FOR DEVELOPING AN EFFECTIVE METHOD FOR CONTACT INVESTIGATIONS

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Abstract [Purpose] To evaluate the various transmission routes of tuberculosis in an outbreak among young adults in order to develop an effective method for contact investigations.

[Method] We reviewed the records of 21 tuberculosis patients involved in an outbreak of tuberculosis; the records were collected by conventional epidemiological studies. *Mycobacterium tuberculosis* isolates were genotyped using IS6110-based restriction fragment length polymorphism (RFLP).

[Result] The index patient was a 26-year-old man whose 32-year-old brother was identified as the source patient of tuberculosis through a contact investigation. Investigation of their contacts led to the identification of 10 tuberculosis patients. Further, 5 more patients with only casual contact with the index or source patients developed tuberculosis 18–25 months after identification of the index patient. The RFLP analysis of strains obtained from these 5 patients as well as the index and source patients revealed an identical pattern. Further, 4 persons, among those who had epidemiological links with some of the above-mentioned 5 patients, developed tuberculosis 22–34 months after identification of the index patient.

All 21 patients were relatively young. In total, 15 strains obtained from these patients were sent for the RFLP analysis, all of which showed an identical pattern. The epidemiological links were categorized into a household environment, an entertainment area, a university, a music band, and a construction site.

[Conclusion] Molecular epidemiology can provide insights into the process of tuberculosis transmission, which may otherwise go unrecognized by conventional contact investigations. Additionally, it can play an important role in identifying places of tuberculosis outbreaks and routes of transmission in a contact investigation.

Key words: Tuberculosis, Outbreak, Contact investigation, Young adult, RFLP, Molecular epidemiology

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Case Report

A CASE OF TUBERCULOUS PERITONITIS ACCOMPANIED BY
LYMPHADENITIS IN A PATIENT WITH LIVER CIRRHOSIS IN WHICH
LYMPH NODE BIOPSY WAS USEFUL FOR ESTABLISHING THE DIAGNOSIS

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Abstract A 62-year-old woman with liver cirrhosis developed ascites. She had been previously treated with a combination of interferon and ribavirin therapy. The ascites was bloody and of exudative nature. Radiological examinations showed supraclavicular, axillar, and mediastinal lymphadenopathy. Biopsy of the axillar lymph node was performed because of suspected malignancy, and the results showed that the lymph node had granulomatous inflammation with caseous necrosis and Langhans giant cells, suggestive of mycobacterial infection. Furthermore, a DNA sequence specific to *Mycobacterium tuberculosis* was recovered from the same lesion, leading to a diagnosis of tuberculous lymphadenitis. The ascites and the lymphadenopathy subsided with anti-tuberculosis chemotherapy. Although bacilli were not detected in the ascites, a high level of adenosine deaminase in the ascites, the coexistence of tuberculous lymphadenitis, and the response to anti-tuberculosis agents supported the diagnosis of tubercu-

lous peritonitis. Although tuberculous peritonitis is often difficult to diagnose, lymph node biopsy was useful to establish the diagnosis in the present case.

Key words: Tuberculous peritonitis, Liver cirrhosis, Ascites, Tuberculous lymphadenitis, Adenosine deaminase, Lymph node biopsy

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Case Report

A CASE OF MILIARY TUBERCULOSIS COMPLICATED BY
DISSEMINATED INTRAVASCULAR COAGULATION
AND ACUTE RESPIRATORY DISTRESS SYNDROME SUCCESSFULLY TREATED
WITH RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN

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¹Seiji HAYASHI, and ¹Katsuhiro SUZUKI

Abstract A 67-year-old woman was referred to our hospital for persistent fever and dyspnea. Chest X-ray revealed diffuse reticulonodular shadows and high-resolution computed tomography showed randomly distributed small nodules. Examination of sputum and urine revealed acid-fast bacilli, which were later confirmed as *Mycobacterium tuberculosis* sensitive to all drugs. Laboratory tests revealed thrombocytopenia, an elevated concentration of fibrin degradation products, and severe hypoxemia. We therefore diagnosed her with miliary tuberculosis complicated by acute respiratory distress syndrome (ARDS) and disseminated intravascular coagulation (DIC). After admission, her status rapidly worsened and she required mechanical ventilation. Treatment with recombinant human soluble thrombomodulin (rTM) and high-dose methylprednisolone was started in addition to the antituberculosis chemotherapy. The patient's condition gradually improved and she was weaned from ventilation on day 30. She was discharged on day 92. It is generally thought that prognosis of miliary tuber-

culosis complicated by DIC and ARDS is very poor. A recent report suggested that rTM is effective for DIC and ARDS secondary to sepsis. This is the first report of miliary tuberculosis complicated by DIC and ARDS successfully treated with rTM.

Key words: Miliary tuberculosis, Disseminated intravascular coagulation, Acute respiratory distress syndrome, Thrombomodulin

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Case Report

A CASE OF ATYPICAL DRUG-INDUCED HYPERSENSITIVITY SYNDROME CAUSED BY ISONIAZID

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and Takeshi ISOBE

Abstract A 43-year-old man developed fever, systemic erythema, and hepatic dysfunction approximately 1 month after initiating treatment with oral allopurinol and anti-TB drugs. The high fever, skin rash, headache, vomiting, and general malaise aggravated even after discontinuation of the anti-TB drugs and allopurinol, and they continued for more than 2 weeks. Hence, the patient was diagnosed with atypical drug-induced hypersensitivity syndrome. Oral prednisolone was introduced at a dosage of 65 mg, and the systemic symptoms rapidly subsided. Drug lymphocyte stimulation test was positive for isoniazid and oxypurinol, a metabolite of allopurinol. The prednisolone dosage was gradually reduced with 3–7 day intervals, and the patient was discharged on day 31 without any recurrence of the symptoms. Although high fever and erythema occurred again upon resumption of isoniazid,

the symptoms gradually improved with oral prednisolone. Finally, the patient was diagnosed with atypical drug-induced hypersensitivity syndrome caused by isoniazid.

Key words: Drug-induced hypersensitivity syndrome, Isoniazid, Oxypurinol, Drug lymphocyte stimulation test

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TUBERCULOSIS ANNUAL REPORT 2010

— (7) Tuberculosis Characteristics upon Diagnosis—2 —

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Abstract From 2007 to 2010, 229 newly notified tuberculosis (TB) cases with HIV infection were reported. These cases were detected in 204 (89.1%) male and 25 (10.9%) female patients; 50 (21.8%) of these patients were foreigners. The present TB surveillance system does not provide reliable data on whether HIV tests were performed for TB cases; therefore, we report only those TB patients with HIV infection.

In 2010, the proportion of newly notified TB cases with diabetes mellitus was 13.3% (3,085/23,261); diabetes was observed in 15.4% of male patients and 9.7% of female patients.

In 2010, drug susceptibility test (DST) results were obtained for 8,380 (72.9%) of 11,495 culture-positive pulmonary TB cases through the TB surveillance system. The proportion of multi-drug resistant TB (MDR-TB), isoniazid resistance, and rifampicin resistance among the newly identified cases was 0.5%, 4.1%, and 0.7%, respectively. Among previously tested

cases, the proportion was 3.9%, 11.4%, and 5.2%, respectively. Resistance thus appears to have remained stable over the past 4 years (2007–2010). From 2007 to 2010, among the new pulmonary TB cases in foreign nationals, MDR-TB was observed in 2.9% of male patients and 4.2% of female patients.

Key words: Tuberculosis, Sex, Age, Foreigner, HIV, Diabetes mellitus, Anti-tuberculosis drug susceptibility test, Multi-drug resistance

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The 87th Annual Meeting President Lecture

PRESENT AND FUTURE OF TUBERCULOSIS CARE IN REGIONS

Eriko SHIGETO

Abstract As the incidence of active tuberculosis in Japan declines and the healthcare environment changes, restructuring of the medical care system for tuberculosis is required. According to a questionnaire survey in Hiroshima Prefecture, experiences in tuberculosis (TB) care and knowledge, such as standard treatment and DOT, is insufficient in the local medical institutions designated for tuberculosis care. Regional coordination between the tuberculosis hospital and the regional private practitioners will be one of the important issues in proper TB care. In order to strengthen coordination, Higashihiroshima Medical Center (HMC) collaborated with Onomichi Medical Association and the health center having jurisdiction over the area (Tobu Health Center) to create liaison clinical paths for doctors, a booklet for patient education and a medication record named "DOTS note". These liaison paths were provided to the regional practitioner from the health center on discharge and referral from HMC. After the start of regional cooperation, treatment outcome of the cohort of sputum smear positive pulmonary tuberculosis in the region were improved: success; 37.0% to 53.3% (cured; 0% to 40.0%, completed; 37.0% to 13.3%), treatment more than 12 months; 17.4% to 6.7%, died 37.0% to 26.7%. It is considered from experience of the regional cooperation in Hiroshima that regional medical cooperation using liaison paths is helpful to provide proper TB care.

Treatment of patients with serious complication(s) is

another issue in TB care. For example, only a few TB hospitals can treat the patient who needs hemodialysis, on the other hand, most general hospitals do not treat TB patients, because they have no beds and little knowledge.

I think the following measures are effective and necessary for the future TB care: 1) one or more of the general hospitals in each region should provide one or more air-controlled bed(s) to treat TB patients, which can be also used for patients with suspected airborne infectious disease, 2) cooperation between tuberculosis experts and general physicians is necessary to provide standard TB care, 3) Rapid communication between TB experts and regional health centers to provide concrete information such as liaison clinical paths, and finally, 4) government commitment is needed to promote the above measures.

Key words: Regional coordination, Liaison clinical path, Community DOTS, Tuberculosis beds

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PATIENT-CENTERED MEDICINE FOR TUBERCULOSIS MEDICAL SERVICES

Chairpersons: ¹Akira FUJITA and ²Tomoyo NARITA

Abstract The 2011 edition of Specific Guiding Principles for Tuberculosis Prevention calls for a streamlined medical services system capable of providing medical care that is customized to the patient's needs. The new 21st Century Japanese version of the Directly Observed Treatment Short Course (DOTS) expands the indication of DOTS to all tuberculosis (TB) patients in need of treatment. Hospital DOTS consists of comprehensive, patient-centered support provided by a DOTS care team. For DOTS in the field, health care providers should select optimal administration support based on patient profiles and local circumstances.

In accordance with medical fee revisions for 2012, basic inpatient fees have been raised and new standards for TB hospitals have been established, the result of efforts made by the Japanese Society for Tuberculosis and other associated groups.

It is important that the medical care system be improved so that patients can actively engage themselves as a member of the team, for the ultimate goal of practicing patient-centered medicine. We have organized this symposium to explore the best ways for practicing patient-centered medicine in treating TB. It is our sincere hope that this symposium will lead to improved medical treatment for TB patients.

1. Providing patient-centered TB service via utilization of collaborative care pathway: Akiko MATSUOKA (Hiroshima Prefectural Tobu Public Health Center)

We have been using two types of collaborative care pathway as one of the means of providing patient-centered TB services since 2008. The first is the clinical pathway, which is mainly used by TB specialist doctors to communicate with local

practitioners on future treatment plan (e.g. medication and treatment duration) of patients. The clinical pathway was first piloted in Onomichi district and its use was later expanded to the whole of Hiroshima prefecture. The second is the regional care pathway, which is used to share treatment progress, test results and other necessary patient information among the relevant parties. The regional care pathway was developed by the Tobu Public Health Center. It is currently being used by several other public health centers in Hiroshima.

Utilization of these two pathways has resulted in improved adherence, treatment being offered at local clinics, shorter hospitalization and better treatment outcomes.

2. Patient-centered DOTS in Funabashi-city: Akiko UOZUMI (Funabashi-city Public Health Center)

In Funabashi-city, all TB patients, including those with LTBI, are treated under DOTS which recognizes and tries to accommodate the various different needs of each individual patient. For example, various types of DOTS are offered, such as pharmacy-based DOTS and DOTS supported by caregivers of nursing homes. This enables public health nurses to take into consideration both the results of risk assessment and convenience for the patient, and choose DOTS which most effectively support the patient. Furthermore, DOTS in principle is offered face-to-face, so that DOTS providers may not only build relationship of trust with the patient, but also to collect and analyze the necessary information regarding the patient and respond timely when problems arise. Such effort has directly contributed to improved default and treatment rate.

3. Hospital DOTS and clinical path for the treatment of

tuberculosis: Kentaro SAKASHITA, Akira FUJITA (Tokyo Metropolitan Tama Medical Center)

We introduced a version of hospital DOTS at Tama Medical Center (formerly Fuchu Hospital) in 2004. As part of this three-stage version, patients are allowed to progress to the next stage if they meet the step-up criteria. Following the introduction of this hospital DOTS, the occurrence of drug administration-related incidents decreased and support for patient adherence became easier for health care workers than before. In 2006, we developed a clinical path based on this hospital DOTS with consistent eligibility criteria for patients. This clinical path helped increase the efficiency of medical services in the TB ward. In conclusion, a patient's initiative for tuberculosis treatment can be supported through our hospital's TB treatment system.

4. Survey of TB patients' understanding and satisfaction of hospital DOTS: Yoko NAGATA, Minako URAKAWA, Noriko KOBAYASHI, Seiya KATO (Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association)

We surveyed the satisfaction and understanding of recently discharged TB patients regarding DOTS to analyze how to better implement DOTS. The questionnaire consisted of nine items covering knowledge of TB, comfort in talking to and asking questions of the medical staff, explanations given to family members, and motivation for continuing medication. Two hundred and eight of the 228 patients who accepted the questionnaire responded (response rate: 91.2%).

The level of understanding and satisfaction tended to be higher among patients in hospitals that employed a primary

nursing system, more coverage and duration of DOT, and audiovisual materials for patient education. The level of understanding and satisfaction also tended to be slightly higher among institutions that conducted in-hospital conferences and collaborated with public health centers more frequently.

5. Medical cooperative system against tuberculosis elimination: Dai YOSHIZAWA (Tuberculosis and Infectious disease control division, Ministry of Health, Labour and Welfare)

There are 3 points we should consider. First, despite one of the intermediate burden countries, emphasis for infectious incidence is insufficient. Besides new incidence decreases gradually, increased ratio of the elderly causes necessity of implementation against each complications. The second is how find infectious one, especially from high burden countries, before they spread it. Final, unspecific symptoms suffer the patients and medical staff. It's the key of implementation that spread of tuberculosis must be caused by delayed diagnosis.

Key words: DOTS, Patient-centered medicine, Hospital DOTS, Regional partnership

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—————The 87th Annual Meeting Symposium—————

FOLLOW-UP DISCUSSION ON RESTRUCTURING THE MEDICAL-SERVICE SYSTEM

Chairpersons: ¹Seiya KATO and ²Arisu KAMADA

Abstract The Japan Tuberculosis Society organized symposia on restructuring the medical-service system at the 84th and 86th annual meetings. These symposia clarified the following issues and concerns.

It is becoming difficult to maintain tuberculosis beds in wards in many areas, since beds required for tuberculosis are declining due to the decreasing incidence of tuberculosis and shortened hospitalization periods. The extremely poor profitability of medical practices has caused closure of tuberculosis wards. A highly urbanized area may have a shortage of tuberculosis beds, while some rural areas have the problem of poor access to hospitalization. Aging of tuberculosis patients causes an increase in the number of patients with serious complications that are sometimes difficult to treat within a prefectural jurisdiction. Infection control for multi-drug resistant tuberculosis needs to be solid. To address these issues and challenges, it will be necessary to restructure the medical-service system for tuberculosis.

The Prevention Guideline addressed in May 2011 by the Ministry of Health, Labour, and Welfare mentions that the medical-service system should seek to ensure enough tuberculosis beds and to realize patient-centered medical service. The future directions should be 1) ensuring a core hospital for tuberculosis treatment at the prefectural level, 2) ensuring a principal hospital for treating tuberculosis patients with serious complications in an area, 3) ensuring the treatment environment is suitable to individual patient conditions, 4) formulating a regional coordination mechanism with a core hospital at the center in each area, and 5) achieving complete infection control. This symposium was organized based on discussions in the previous symposia to present points necessary to realize the future medical-service system described in the Prevention Guideline.

When constructing a new hospital or renovating a ward, attention must be paid to infection control and amenities for tuberculosis patients whose hospitalization is often longer than patients of other diseases. There is no official standard for a facility with tuberculosis beds at this moment. Professor Atsuo Kakehi, a hospital architectural expert, discussed the points in a draft of the standard he proposed in his report.

Aging of tuberculosis patients increases the number of patients with serious complications. Ensuring medical service for such patients is a major challenge. The new National Hospital Organization Hokkaido Medical Center was built in March 2010 with tuberculosis wards. Dr. Arisu Kamada reported on infection control and medical practice for patients with serious complications in a general hospital.

Psychiatric diseases including senile dementia are among

the largest problems among tuberculosis complications. The National Hospital Organization Kamo Psychiatric Center, which has model beds for tuberculosis, produced successful outcomes by collaborating with the National Hospital Organization Higashihiroshima Medical Center tuberculosis hospital. Dr. Masahiro Nomura reported on the implementation of DOT and regional collaboration as well as medical practice in his hospital.

An important point in the National Guideline is regional collaboration. Dr. Tadatoshi Suruda from the National Hospital Organization Wakayama National Hospital discussed the status and outcomes from their regional collaboration system in Wakayama Prefecture, the top runner in this area.

Thanks to solid presentation from the speakers and thoughtful comments from the floor, the symposium was very useful for promoting patient-centered medical service, a keyword in the National Guideline.

1. Environment of hospital beds for treating TB patients: Atsuo KAKEHI (Department of Architectural Design, School of Architecture, Kogakuin University)

It is becoming more difficult to configure wards since the number of tuberculosis beds is decreasing. It is therefore necessary to mix general beds and tuberculosis beds in one ward, making it necessary to develop criteria for designing facilities as part of a general ward for isolated space. This paper describes the current care environment of tuberculosis patients and the draft guidelines for a more appropriate hospital environment.

2. Treatment to complications in the patients in the tuberculosis hospital: Arisu KAMADA (National Hospital Organization Hokkaido Medical Center)

Recently, many patients with tuberculosis, especially the elderly, have been exhibiting various complications. It is often difficult to treat complications at a tuberculosis hospital, especially at the old sanatorium hospital. Our hospital is both a tuberculosis hospital and a general hospital in which various complications can be treated. However, such general hospitals are very rare in Japan. Many patients passed away immediately after transferring to a tuberculosis hospital due to inadequate treatment of complications. To avoid repeating such tragedies, continuing treatment of complications without transferring to a tuberculosis hospital should be considered.

3. Tuberculosis care in psychiatry: Masahiro NOMURA (Department of Internal Medicine, National Hospital Organization Kamo Psychiatric Center)

Kamo Psychiatric Center has eight model beds for tuberculosis patients with psychiatric diseases. We retrospectively studied 71 cases of hospital DOTS from 2006 to 2011. There were 33 dementia cases and 30 schizophrenia cases. The standard regimens (A or B) were performed for 68 of the 71 cases. The median duration of hospitalization was six months. Some schizophrenia cases taking antipsychotic medications experienced worse mental symptoms when they started tuberculosis treatment.

4. Medical collaboration for tuberculosis patients' care in region: Tadatoshi SURUDA (National Hospital Organization Wakayama National Hospital)

Complete medical collaboration for tuberculosis patients' care is possible by close cooperation utilizing coordination tools such as the regional critical path among TB hospitals, other medical facilities, welfare organizations, and health centers that function as a coordinator in an area. TB hospitals and

health centers, both major role players in the collaboration scheme, should maintain good ties and share responsibilities. Through establishing close collaboration, medical service for TB patients will be a part of primary practice. It is expected to raise TB awareness among general medical staff and result in early case detection in the area.

Key words: Tuberculosis, Facility standard, Complication, Regional-collaboration system

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