
Review Article

TRANSMISSION OF TUBERCULOSIS (I)

Masakazu AOKI

Abstract BCG vaccination has been given to infants and children so extensively and repeatedly for more than 55 years in Japan that it is very difficult, or often impossible to diagnose tuberculosis infection by tuberculin testing. On the other hand, as the treatment of latent tuberculosis infection has become more and more important recently, diagnosis of infection is becoming more and more important at the occasions of contact survey. However, understanding of the health care workers about transmission of tuberculosis is incomplete frequently at present. This is the reason why the author has written this review. The author has described on the history of the progress of droplet nuclei infection theory, infectivity of tuberculosis by bacteriological status of the patients, impor-

tance of cough, susceptibility of the host, and environmental factor concerning transmission of tubercle bacilli in this issue.

Key words: Tuberculosis transmission, Droplet nuclei infection, Airborne infection, Infectivity of smear positive case, Infectivity of culture positive case, Sensitivity of the host, Compromised host, Air exchange

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Original Article

MOLECULAR EPIDEMIOLOGICAL ANALYSIS BY IS1245
BASED RESTRICTION FRAGMENT LENGTH POLYMORPHISM TYPING
ON CASES WITH PULMONARY *MYCOBACTERIUM AVIUM* DISEASE
OBSERVED IN THE SAME FAMILY

¹Katsuhiko KUWABARA, ²Yasushi WATANABE, ¹Koichi WADA, and ¹Toshiaki TSUCHIYA

Abstract [Introduction] *Mycobacterium avium-intracellulare* complex (MAC) has become one of major human pathogens, however, its routes of transmission and environmental reservoirs causing human infection were not yet elucidated. We reported three families affected by pulmonary *Mycobacterium avium* (*M. avium*) disease. Previous reports on MAC diseases observed in the same family were very rare. The purposes of this study were to investigate whether the infected *M. avium* was the same strain among cases in the same family and to examine the possibility of human-to-human transmission, or infection from exposure to a common environmental reservoir.

[Methods] *M. avium* isolates from nine cases of three families were examined by DNA polymorphism based typing technique, restriction fragment length polymorphism (RFLP) analysis using insertion sequence IS1245 as a probe, to type the strains. Some isolates were subcultured to a single clone.

[Results] All strains isolated from cases in the same family showed different patterns by the RFLP analysis. And not only

simultaneous polyclonal infection but also repeated polyclonal infections were observed in some patients.

[Discussion] The results suggest importance of underlying anti-mycobacterial immunological impairment and defects of local defense rather than virulence of infected strains as the pathogenesis of pulmonary *M. avium* disease.

Key words: *Mycobacterium avium*, Familial pulmonary disease, RFLP, IS1245

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Original Article

DIRECT DETECTION OF RIFAMPICIN RESISTANT *MYCOBACTERIUM TUBERCULOSIS* IN SPUTUM BY LINE PROBE ASSAY (LiPA)

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³Takeshi OGURA, ⁴Hiroko YOSHIDA, ⁵Tetsuya TAKASHIMA, ⁶Masaru NAKAGAWA,
⁶Ryoji MAEKURA, ⁶Toru HIRAGA, and ⁷Toshinori SUETAKE

Abstract [Objectives] To examine the direct detection of rifampicin (RFP) -resistant *Mycobacterium tuberculosis* in sputum by Line Probe Assay (LiPA).

[Materials and methods] We collected 130 sputa and analyzed both by LiPA and the Amplicor *M. tuberculosis* assay. For culture-positive samples, RFP resistance testing was performed and compared with the results by LiPA.

[Results] Eighty two out of 84 *M. tuberculosis* samples were detected by LiPA and all of 10 *Mycobacteria* other than *M. tuberculosis* (MOTT) samples and 36 negative samples were negative by LiPA. The detection rate is same as Amplicor. For culture-positive samples, LiPA showed mutation pattern for all of 22 RFP-resistant strains and wild type pattern for 19 of 20 RFP-sensitive strains. The one remaining showed mixed pattern of wild type and mutation pattern.

[Conclusion] The use of LiPA for sputum could enable early detection of RFP-resistant tuberculosis and seems to be useful for the control of tuberculosis.

Key words: *Mycobacterium tuberculosis*, *rpoB* gene, Rifampicin resistance, Line probe assay, Sputum

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Case Report

**A CASE OF PUBIC TUBERCULOUS OSTEOMYELITIS AND PERICARDITIS
DURING ANTI-TUBERCULOSIS CHEMOTHERAPY**

Minoru OHKOUCHI, Naohiko INASE, Makito YASUI, and Hirotarou MIURA

Abstract 56 year-old man was referred to the department of orthopedics in our hospital for further investigation on right inguinal pain. The patient was initially diagnosed as bacterial myelitis in right pubic bone and was treated with antibiotics. Since his symptom did not improve, the curettage was performed. Histological examination of the pubic bone obtained during the operation showed epithelioid cell granulomas with caseous necrosis, supporting the diagnosis of tuberculous osteomyelitis. Chest X-ray film revealed small nodular lesions in both upper lung fields. Sputum was positive for acid-fast bacilli and Amplified Mycobacterium Tuberculosis Direct Test (TB-MTD) was positive. The diagnosis of pubic tuberculous osteitis and pulmonary tuberculosis was confirmed. Specimens from the pubic bone and sputum were both culture positive for *Mycobacterium tuberculosis*, and bacilli were sensitive to anti-tuberculosis drugs. The antituberculosis chemotherapy was started with INH, RFP, SM and PZA. Symptoms had gradually improved, however 3 months after starting treatment, high fever developed and chest X-ray revealed heart enlargement and bilateral pleural effusion. Pericardial effusion showed exudative nature with lymphocyte

predominancy and high level of ADA, 98.4 U/l. Pleural effusion was transudate. TB-MTD and culture were negative both in pericardial and pleural effusion. Paradoxical reaction was thought to be the cause of pericarditis. TB chemotherapy was continued and pericardial drainage was performed. One month later, fever improved, and pleural effusion and pericardial effusion disappeared.

Transient elevated transaminase was observed, and was thought to be the side effect of anti TB drugs. All symptoms gradually improved, and he was discharged after 6 months TB chemotherapy.

Key words: Pubic tuberculous osteomyelitis, Tuberculosis pericarditis, Tuberculosis pleurisy, Paradoxical reaction

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Case Report

**AN INFANT WITH TUBERCULOSIS WHO PREVIOUSLY CONTACTED WITH
AN INFANT WITH CONGENITAL TUBERCULOSIS**¹Shinya KONDO and ²Gen NISHIMURA

Abstract We report a case of one-year and three-month old male infant with healed tuberculosis who was found by positive tuberculin skin test prior to scheduled BCG vaccination. Abdominal CT imaging revealed calcification in liver, spleen, and lymphonodes along pancreas and hepato-duodenal ligament, despite of normal chest imaging. A temporary intubated infant with congenital tuberculosis and/or his mother with untreated tuberculosis might infect him during his stay in the same NICU when he had digestive disease at three-month old. This report suggests that periodic contact investigation is needed for infants who had contact with the intubated infant with congenital tuberculosis in the same room, since cell-

mediated immunity is not well developed in infants.

Key words: Congenital tuberculosis, Contact investigation, Tuberculous infant, CT imaging

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TUBERCULOUS INFECTION AND BIOLOGICAL RESPONSE IN MAN

Kaoru SHIMOKATA

Abstract The characteristics and function of human lymphocytes in tuberculous morbid site were studied. Exudative-sensitized lymphocytes in tuberculous pleural fluid reacted to the specific antigen more effectively and produced higher titers of cytokines including interferon γ (IFN- γ) than circulating lymphocytes. CD4+/CD8- T-cell subset is responsible for the antigen-specific IFN- γ production in pleural T lymphocytes of patients with tuberculous pleurisy. Thus, activated T lymphocytes concern the production of cytokines at the morbid site and they effectively exert local cellular immunity through the action of such cytokines. Immunofluorescence study showed increased production of inducible nitric oxide synthase (iNOS) and peroxynitrite in BCG-inoculated human alveolar macrophages (AM). Reverse transcriptase-polymerase chain reaction methods also revealed the higher expression of iNOS-coding mRNA. Colony assay demonstrated that human AM effectively killed BCG in their cytoplasm. However, treatment of AM with NG-monomethyl-L-arginine monoacetate resulted in markedly reduced killing activity. These results clearly show that BCG-induced NO and its reactive product with the oxygen radical, peroxynitrite, could play an important role in BCG killing in human AM.

We measured the pleural concentrations of IFN- γ , interferon- γ -inducing cytokines; interleukin (IL)-12 and IL-18 and interferon- γ -inducible chemokines; IFN- γ -inducible protein of 10 kDa (IP-10), monokine induced by IFN- γ (Mig), and IFN-inducible T cell α chemoattractant (I-TAC). These cytokines and chemokines in tuberculous pleural effusions were much higher than those in malignant pleural effusions. These findings indicate that IFN- γ plays an important role in the cell mediated immunity in tuberculosis.

Key words: Tuberculosis, Cytokine, Interferon- γ , Chemokine

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