Original Article

EFFICACY OF TUBERCULOSIS CONTACTS INVESTIGATION AND TREATMENT, ESPECIALLY OF PREVENTIVE THERAPY IN INFANTS AND YOUNG CHILDREN

Shinya KONDO and Masaki ITO

Abstract [Background] Although large clinical trials reported in 1960s suggested that preventive therapy in subjects with tuberculosis (TB) infection reduces the risk of developing TB by 70−90%, the therapy in our TB clinic seems to be more effectiveness.

[Objective] We retrospectively evaluated the efficacy of the present contacts investigation, especially of preventive therapy for further improvement of TB control for children.

[Methods] We examined 273 asymptomatic infants and children younger than five years who had household contacts with active TB patients and visited our clinic for contact investigation. After the diagnosis at the first visit to our TB clinic, they were treated and/or observed for at least two years to assess whether contact investigations and following treatment are appropriate. Since infants less than a year are underdeveloped in cell-mediated immunity and their tuberculous lymphadenopathy can be overlooked on standard chest radiographs, chest CT scans were added.

[Results] At their first visit, 60 (22%) out of 273 subjects were diagnosed as TB, and 37 (14%) were suspected as TB. We treated them by combinations of anti-TB medicines including isoniazid and rifampin for six to 12 months, and they did not relapse during the observation period. Twenty-six subjects (9%) were diagnosed uninfected. However, a three-year-old girl developed bilateral hilar lymphadenopathy two months later when the reexamination was done. A hundred and fifty subjects (55%) were diagnosed to have TB infection. They received preventive therapy with isoniazid (10 mg/kg/day) for six months. Among them, a four-month-old boy developed TB disease soon after starting to take isoniazid and was treated by the combination of anti-TB medicines. Other 149 subjects completed the therapy, and none of them developed disease during the observation period. There was no increase in serum GOT and/or GPT to >100 IU/L within one month after starting to take isoniazid.

[Conclusion] The present contacts investigations and treatments in our TB clinic are useful ways to find out and control TB diseases and infections, and it might be suggested to start the six-months preventive therapy after active TB has been ruled out in all infants and children who had close contacts with active TB patients for preventing TB disease and latent TB infection in the future even their clinical and laboratory examinations do not suggest infection.

Key words : Tuberculosis in infants and young children, Household contact, Contacts investigation, Primary infection, Preventive therapy, Latent tuberculosis infection

Division of Respiratory Disease, Tokyo Metropolitan Children's Hospital

Correspondence to : Shinya Kondo, Division of Respiratory Disease, Tokyo Metropolitan Children's Hospital, 1−3−1, Umezono, Kiyose-shi. Tokyo 204−0024 Japan.
(E-mail : shykondo@chp-kiyose-tokyo.jp)

AGRANULOCYTOSIS DUE TO ANTI-TUBERCULOSIS DRUGS INCLUDING ISONIAZID (INH) AND RIFAMPICIN (RFP)

— A Report of Four Cases and Review of the Literature —

Yuichiro SHISHIDO, Naohiro NAGAYAMA, Kimihiko MASUDA, Motoo BABA, Atsuhisa TAMURA, Hideaki NAGAI, Shinobu AKAGAWA, Yoshiko KAWABE, Kazuko MACHIDA, Atsuyuki KURASHIMA, Hikotaro KOMATSU, and Hideki YOTSUMOTO

Abstract We experienced 4 cases of agranulocytosis due to anti-tuberculosis drugs (rifampicin [RFP], isoniazid [INH], ethambutol [EB], streptomycin [SM] or pyrazinamide [PZA]) among some 6,400 tuberculosis patients who underwent chemotherapy over the past 20 years from 1981 to 2002 in our hospital, and the incidence rate of agranulocytosis was estimated at 0.06%. The 4 cases of agranulocytosis were as follows.

[Case 1]

A 51-year-old woman with right chest pain and fever was admitted to our hospital on Jan 4, 2001. The white blood cell (WBC) count was 5,200/μl. The tubercle bacilli were cultured in her sputum. The treatment with INH 0.3, RFP 0.45, EB 0.75, PZA 1.2 g/day, allopurinol and teprenone was started on Jan 13. Pyrazinamide and allopurinol were stopped because of hyper-uric acidemia on Feb 7. Agranulocytosis and eosinophilia (WBC 1,300 [Neut 1%, Ly 57%, Eos 35%]) developed on Feb 13. All drugs were withdrawn and G-CSF drug nartograstim 100 μg was injected subcutaneously for 3 days. The WBC recoverd to normal level and she was thereafter treated with INH, EB and Levofloxacin (LVFX) without any further trouble. Agranulocytosis in this case was supposed to be due to RFP.

[Case 2]

A 66-year-old man who had had nephrotic syndrome and hypothyroidism and has been treated with prednisolone 10 mg/day was admitted to our hospital on Aug 9, 2000 because of miliary tuberculosis. The tubercle bacilli were cultured in his sputum and the treatment with INH 0.3, RFP 0.45, and EB 0.75 g/day were started on Aug 10, but it was witdrawn on Aug 17 because of general skin eruption. After re-starting treatment with EB and INH on Aug 24, RFP was added in

small dosage (0.05g) on Oct 12, but agranulomatosis (WBC 2,300/μl [Neut 2%]) developed on Nov 21, and all drugs were withdrawn again. The G-CSF drug filgrastim was used once subcutaneously, and WBC recovered immediately. He was thereafter treated with INH, EB, LVFX successfully. Agranulocytosis was supposed to be due to RFP.

[Case 3]

A 60-year-old woman without symptoms had abnormal chest roentgenograph, and consulted with our hospital on Aug 26, 2002. The broncho-alveolar lavage fluid was smear and culture-negative, but PCR-TB positive, and the case was diagnosed as pulmonary tuberculosis. Treatment with INH 0.3, RFP 0.45, EB 0.75, PZA 1.2 g/day, alloprinol 300 mg and rebamipide 300 mg/day was started on Sept. 5, 2002. Late in September, she complained of appetite loss. The laboratory data on Oct 3 revealed WBC 900/μl (Neut 1%, Ly 94%), aspartate aminotransferase (AST) 199 IU/*l*, and alanine aminotransferase (ALT) 253 IU/*l*, showing agranulocytosis and drug-induced hepatitis. The chemotherapy was immediately withdrawn and she was admitted to our hospital on the next day. Glycyrrhizin derivative (SNMC) 40 m*l* was injected for 5 days, and WBC recovered, and AST and ALT also became normal.

[Case 4]

A 60-year-old man was admitted to our hospital on March 11, 1981 because pulmonary tuberculosis had recurred. He had been treated with SM, PAS and INH in 1973 for pulmonary tuberculosis. On admission examination of blood count and blood chemistry were normal. Treatment with RFP, INH and SM was started on March 11. He stopped out from the hospital on April 17, but in a few days he returned back with sore throat, lower lip swelling and gingival bleeding. Blood cell count on April 24 showed pancytopenia with RBC 226, Hb 7.5, WBC 800 (Ly 96%, Eos 4%) and Plt 10,000/μl. The bone-marrow showed NCC (nuceated cell count) of 5,500, and megakaryocyte 0. Thereafter ground glass appearance shadows were seen on the whole lung field, and he died May 26. Autopsy showed generalized aspergillosis. It was strongly suspected that either of RFP, INH or SM was responsible for his pancytopenia.

We collected another 10 cases of agranulocytosis due to anti-tuberculosis drugs in the world wide literature, and found men/women ratio 5/8 (in one case gender was not known), the duration of chemotherapy before appearance of agranulocytosis 1−3 months, no change in the lymphocyte count of the peripheral blood, and the accompanying of another allergic signs such as skin eruption, blood eosinophilia or drug-induced hepatitis in some cases, and these findings suggest that the mechanism of agranulocytosis due to anti-tuberculosis drugs was allergic in nature.

Key words : Rifampicin, Isoniazid, Agranulocytosis, Lymphocyte, Tuberculosis

Department of Respiratory Medicine, Tokyo National Hospital

Correspondence to : Naohiro Nagayama, Department of Respiratory Medicine, Tokyo National Hospital, 3−1−1, Takeoka, Kiyose-shi, Tokyo 204−8585 Japan.
(E-mail : nagayama@tokyo.hosp.go.jp)

Original Article

A SURVEY ON THE ONSET OF TUBERCULOSIS IN NURSING HOMES

[1]Shinji SHISHIDO, [1]Hitoshi HOSHINO, [1]Nobukatsu ISHIKAWA,
[1]Toru MORI, and [2]Noriko TAKASATO

Abstract [Purpose] To obtain the informations how to promote early detection and prevention of nosocomial infection of tuberculosis in nursing homes for the elderly.

[Subject] Fifteen elderly patients who developed tuberculosis from 1998 to 2002 at nursing homes within a certain health center jurisdiction area which has a total of 23 nursing homes were investigated.

[Method] We collected informations on these 15 patients concerning the clinical conditions, details of contact examinations and status of chemoprophylaxis by using TB registration card in the health center and interviewing with the members of staff of the nursing homes and hospitals, and case conferences conducted at the health center.

[Results] Four patients died within 10 days after the diagnosis due to the delay in referring them to doctors. The most common symptoms leading to the detection was fever, followed by cough.

[Discussion] Early diagnosis is the key to prevent early death and nosocomial infection of tuberculosis in nursing homes. A similar study will be useful at each health center or region to improve the tuberculosis control in nursing homes.

[Conclusion] Tuberculosis control programs in nursing homes should be strengthened. The staff of nursing homes should be trained for closer observations of the elderly about their health conditions such as fever and cough, and their early reference to physicians when such symptoms were observed. Two step tuberculin skin tests to the staff is also important for the contact investigations.

Key words: Nursing home, Tuberculosis, Actual status of onset of disease, Prevention from infection, Measure of tuberculosis

[1]Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, [2]Tokyo Metropolitan Akikawa Health Center (Tokyo Metropolitan Mitaka Musashino Health Center at present)

Correspondence to: Shinji Shishido, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, 3−1−24, Matsuyama, Kiyose-shi, Tokyo 204−8533 Japan.
(E-mail: sshishido@jata.or.jp)

Case Report

AN ADULT CASE OF HYPOPLASIA OF THE LEFT LUNG DISCLOSED BY PNEUMONECTOMY FOR PULMONARY *M. AVIUM* COMPLEX INFECTION ASSOCIATED WITH INTRACTABLE PNEUMOTHORAX

[1]Seiyu HIRATA and [2]Eiichi TSUJI

Abstract A case of W-P-W syndrome complicated with pulmonary hypoplasia disclosed by pneumonectomy for pulmonary *Mycobacterium avium* complex infection associated with intractable pneumothorax was reported. A male patient aged 52 years consulted our clinic with chief complaints of cough and abnormal shadows on his chest radiogram, which was consistent with mycobacteriosis on his left lung. MAC infection was soon confirmed by sputum examination and he was treated with RFP, EB, INH combined with CAM. In spite of the chemotherapy, sputum examination of the patient remained positive. Furthermore, eleven months after initiating the treatment, an intractable pneumothorax concurrent with a large dead space at the left lower lung field was consistently observed on his chest radiogram. Therefore, he was first treated by video assisted thoracoscopic surgery, but soon relapsed which led to tention pneumothorax gradually. Consequently, a left pneumonectomy had to be performed and the following developmental abnormalities combined with pathological changes caused by MAC infection were disclosed: concerning the upper lobe, defect of lingula, formation of a peripheral type of congenital air-filled parenchymal cyst measuring 5 × 6 cm in S^3, and atelectatic induration caused by MAC infection on the remaining part of the upper lobe where strong adhesion was seen between the chest wall and the lung. Concerning the lower lobe, congenital shortening of visceral pleura, mainly mediastinal surface, causing marked deformity of the lower lobe with elevation of margo inferior. This created a large dead space between the lower lobe and diaphragma, and formation of a walnut-sized nest of atelectatic induration caused by MAC infection in S^6. The patient's post-operative clinical course was uneventful and his arterial blood gas was elevated from 76 torr to 99.2 torr. He was discharged three weeks after the operation.

Several controversial issues relating to this case were discussed; the predisposition existing on the hypoplastic lung to MAC infection, the possible reason why the congenital pulmonary cyst was not involved in MAC infection, the location of perforation of the upper lobe that caused intractable pneumothorax, and the difficulty in diagnosing congenital air-filled bullous parenchymal cyst by current conventional chest radiogram.

Key words: Pulmonary *Mycobacterium avium* complex infection, Pulmonary hypoplasia, Congenital pulmonary cyst, W-P-W syndrome, Atelectatic induration

[1]Tateyama Hospital, [2]Third Department of Surgery, Tokyo University School of Medicine

Correspondence to: Seiyu HIRATA, Tateyama Hospital, 196 Nagasuka, Tateyama-shi, Chiba 294−0037 Japan.

The 78th Annual Meeting Symposium

PNEUMOCONIOSIS AND MYCOBACTERIAL INFECTION

Chairpersons: [1]Masamitsu KIDO and [2]Mitsunori SAKATANI

Abstract This symposium was organized to provide recent informations concering pneumoconiosis and mycobacterial diseases in Japan. Pneumoconiotic workers have been decreasing in number and in severity because of change in industrial structure and improvement of occupational health measures. But radiological figures of dust exposed worker are going to be complex and be difficult for diagnosis due to aging, smoking and of complicated respiratory and non-respiratory diseases. Major complications such as pulmonary tuberculosis and tuberculous pleurisy are decreasing but non-tuberculous mycobacterial infections have become common among dust exposed workers.

Dr. Katsuhiro Suzuki (National Kinki-Chuo Hospital) reported pulmonary tuberculosis complicated with pneumoconiosis. A few reports regarding tuberculosis with pneumoconiosis have been published in recent years, particularly in Japan. Thus, clinical characteristics of the cases in our hospital between 1998 and 2003 were summarized here. There were 22 such patients, who consisted of 21 men and one woman and were 49 to 91 years old. There were 19 cases with silicosis, two cases with asbestosis, and one case with siderosis. Bilateral and cavitary lesions in a chest XP were revealed in 82% and 29% of the cases, respectively. Standard chemotherapeutic regimens consisted of three or four drugs with a prolonged period were found to be as effective as that for healthy subjects, judging from the sputum conversion rate after 8 week treatment.

Dr. Toshiyuki Yamauchi (Keihai Rosai Hospital) reported, based on autopsy findings, trends in combined-type tuberculosis accompanying pneumoconiosis. The study period was divided into first (1963−1980) and second (1981−2000) stages based on year of patients death. To assess the therapeutic efficacy of antituberculosis agents, patients with combined-type tuberculosis were pathologically divided into those with active tuberculosis and those with inactive tuberculosis. The incidence of active tuberculosis during the second stage was significantly lower than that during the first stage. In both first and second stages, the average age of death for patients with inactive tuberculosis was older than that for those with active tuberculosis. It was shown that active combined-type tuberculosis was resistant to antituberculosis therapy and the prognosis of those patients tends to be poor. But for all patients with active and inactive combined-type tuberculosis, the average age of death was comparable to that of patients without tuberculosis in each stage. The results indicated that the antituberculosis agents were effective to combined-type tuberculosis.

Dr. Kiyonobu Kimura (Iwamizawa Rosai Hospital) carried out retrospective studies on some clinico-epidemiologic problems in the cases accumulated in his hospital during the past 49 years. Since his cases consist of various different pathological changes, he has adopted the term "pneumoconiosis complicated with pulmonary tuberculosis" instead of silico-tuberculosis. The results were summarized as follows:

(1) The rates of active pulmonary tuberculosis out of 1051 total dead cases were 43.8% (28/64) from 1955 to 1964, 28.8% (62/215) from 1965 to 1974, 24.7% (93/376) from 1975 to 1984, and 10.1% (40/396) from 1985 to 1994.

(2) The rates of those who died of pulmonary tuberculosis were 17.2% (11/64) from 1955 to 1964, 9.3% (20/215) from 1965 to 1974, 1,9% (7/376) from 1975 to 1984, and 3.3% (13/396) from 1985 to 1994, respectively.

(3) The average age of death of pulmonary tuberculosis has become older and is not significantly different from that of pneumoconiosis patients who died of other cause.

(4) The rate of sputum negative conversion was only 9.1% (3/33) during the first 10 years (from 1955 to 1964). On the other hand, 95% (21/22) in the recent 9 years (from 1993 to 2002).

(5) Out of the 104 autopsy cases in whom pneumoconiosis and tuberculosis were diagnosed pathologically, 64 cases were combined form of tuberculosis, and other 40 cases were complicated form of tuberculosis.

Dr. Hiroki Morita (Asahi Rosai Hospital) studied the nontuberculous mycobacteria (NTM) in the patients with pneumoconiosis and the clinical courses of the 4 types of pneumoconiosis complicated with NTM pulmonary disease. NTM were detected in the 73 (29%) of 252 pneumoconiosis. The 14 species (*M. gordonae*, *M. avium*, *M. terrae*, *M. fortuitum*, *M. nonchromogenicum*, *M. peregrinum*, *M. intracellulare*, *M. szulgai*, *M. abscessus*, *M. simiae*, *M. chelonae*, *M. scrofulaceum*, *M. xenopi*, *M. triviale*) were identified. In the long-term follow-up study of the pneumoconiosis patients complicated by NTM pulmonary disease, it was very difficult to catch the onset of NTM pulmonary disease because the clinical signs and symptoms were nonspecific and the radiographic findings moved very slowly.

Dr. Mitsunori Sakatani (National Kinki-Chuo Hospital) reviewed the laws related safety and health for dust exposed workers, pneumoconiosis and tuberculosis, and he pointed out importance for prevention, diagnosis, treatment and compensation.

Key words: Pneumoconiosis, Silicosis, Tuberculosis, Non-tuberculous mycobacteria, Related laws

[1]Department of Respiratory Disease, University of Occupational & Environmental Health Japan, [2]Department of Internal Medicine, National Kinki-Chuo Hospital for Chest Diseases

Correspondence to: Masamitsu Kido, Department of Respiratory Disease, University of Occupational & Environmental Health Japan, 1−1, Iseigaoka, Yahatanishi-ku, Kitakyushu-shi, Fukuoka 807−8555 Japan.
(E-mail: mkid@med.uoeh-u.ac.jp)

TUBERCULOSIS IN COMPROMISED HOSTS

Chairpersons: [1]Fumio YAMAGISHI and [2]Kaoru SHIMOKATA

Abstract Recent development of tuberculosis in Japan tends to converge on a specific high risk group. The proportion of tuberculosis developing particularly from the compromised hosts in the high risk group is especially high. At this symposium, therefore, we took up diabetes mellitus, gastrectomy, dialysis, AIDS and the elderly for discussion. Many new findings and useful reports for practical medical treatment are submitted; why these compromised hosts are predisposed to tuberculosis, tuberculosis diagnostic and remedial notes of those compromised hosts etc. It is an important question for the future to study how to prevent tuberculosis from these compromised hosts.

1. Tuberculosis in diabetes mellitus: aggravation and its immunological mechanism: Kazuyoshi KAWAKAMI (Department of Internal Medicine, Division of Infectious Diseases, Graduate School and Faculty of Medicine, University of the Ryukyus)

It has been well documented that diabetes mellitus (DM) is a major aggravating factor in tuberculosis. The onset of this disease is more frequent in DM patients than in individuals with any underlying diseases. However, the precise mechanism of this finding remains to be fully understood. Earlier studies reported that the migration, phagocytosis and bactericidal activity of neutrophils are all impaired in DM patients, which is related to their reduced host defense to infection with extracellular bacteria, such as *S. aureus* and *E. colli*.

Host defense to mycobacterial infection is largely mediated by cellular immunity, and Th1-related cytokines, such as IFN-γ and IL-12, play a central role in this response. It is reported that serum level of these cytokines and their production by peripheral blood mononuclear cells (PBMC) are reduced in tuberculosis patients with DM, and this is supposed to be involved in the high incidence of tuberculosis in DM. Our study observed similar findings and furthermore indicated that IFN-γ and IL-12 production by BCG-stimulated PBMC was lower in poorly-controlled DM patients than that in well-controlled DM patients and healthy subjects. Thus, these clinical data suggest that the high incidence of tuberculosis in DM patients is due to the impaired production of Th1-related cytokines. However, direct evidences to prove this possibility remain to be obtained.

In 1980, Saiki and co-workers reported that host defense and delayed-type hypersensitivity response to *M. tuberculsosis* was hampered in a mouse DM model established by injecting streptozotocin (Infect Immun. 1980; 28: 127−131). We followed their investigation with the similar observations. Interestingly, levels of IFN-γ and IL-12 in serum, lung, liver and spleen after infection were significantly reduced in DM mice when compared with those in control mice. Considered collectively, these results strongly suggest that the reduced production of Th1-related cytokines leads to the susceptibility of DM to mycobacterial infection.

However, it remains to be understood how DM hampers the synthesis of Th1-related cytokines. In our preliminary study, the production of these cytokines by PBMC from DM patients and healthy subjects was not affected under a high glucose condition. Thus, it is not likely that the increased level of glucose directly suppresses the cell-mediated immune responses. Further investigations are needed to make these points clear.

2. A study of gastrectomy cases in pulmonary tuberculosis patients : Takenori YAGI (Division of Thoracic Disease, National Chiba-Higashi Hospital)

Patients who have undergone gastric resection are considered at increased risk of developing pulmonary tuberculosis. I have investigated the role played by gastrectomy in giving rise to pulmonary tuberculosis.

Of 654 pulmonary tuberculosis patients admitted to National Chiba-Higashi Hospital from January 1999 to December 2001, 55 patients (31−84 years old, mean 63.5 ± 12.5 years, 48 males and 7 females) had the history of gastric resection. The incidence of gastrectomy among patients with pulmonary tuberculosis was 8.4 percent. The mean age of gastric resection was 50.2 ± 16.6 years, and the mean interval from gastrectomy to pulmonary tuberculosis was 13.6 ± 11.0 years. On admission to our hospital, 34 out of 55 cases were smear positive by sputum examination for acid-fast bacilli and 39 cases had cavitary lesions on chest X-ray. Gastrectomy was done due to carcinoma of the stomach in 31 cases, gastric and/or duodenal ulcer in 21 cases, adenomatous polyp in two cases, and accidental injury in one case. 52 patients improved, but three cases died due to pulmonary tuberculosis. No one had recurrence of carcinoma of the stomach.

Body weight, Body Mass Index, Prognostic Nutritional Index (PNI; 10 × serum albumin concentration + 0.005 × peripheral lymphocyte count) which was proposed by Onodera, serum albumin level and serum total cholesterol level were lower in the gastrectomy group than in the non-gastrectomy group.

I calculated the odds of tuberculosis among gastrectomy patients to be 3.8 times that of appropriate controls.

This study confirms that gastrectomy is one of the risk factor(s) of tuberculosis. However, whether gastrectomy in itself is a risk factor or whether it is secondarily associated with another risk factor such as underweight status and/or inadequate nutrition following surgery remains unclear.

3. Immunodefficiency and tuberculosis in dialysis patients : Hajime INAMOTO (Division of Dialysis, Keio University School of Medicine)

The patients who have renal insufficiency is fatal, but they can live much longer by dialysis. The number of lymphocytes of the patients whose serum creatinine was 10 mg/d*l* or more has decreased to about 50% of the people who have normal kidney. When the lymphocyte was cultured after it was stimulated with PHA, the DNA synthesis of the patients' lymphocyte was much lower than that of the modest people's.

In the dialysis food, the nutrient such as vitamins, minerals, etc. were lacked. The density of the serum albumin of the dialysis patient has decreased. Many of them were thin when their BMI was examined.

The size of the patients' erythema by the tuberculin test has become small. There were many patients receiving dialysis with erythema but no induration. It means that the delayed skin reaction specific to *Mycobacterium tuberculosis* has decreased among the dialysis patients.

The morbidity rate, the mortality rate and the prevalence of tuberculosis was much higher than the general population. The anamnesis of tuberculosis was also high. Most of those tuberculosis patients appear the disease from the period immediately before the beginning of dialysis to one year after that. That is also the period that patients' number of peripheral blood lymphocyte decreased and the tuberculin reaction positivity rate fell sharply. During the dialysis patients, pulmonary tuberculosis with cavities was minority and extrapulmonary tuberculosis and miliary tuberculosis were remarkably many. People with large reaction against the tuberculin test were better prognosis than those with smaller reaction. It was thought that anorexia, weakening, and a weight decrease were seen when the immunity decreased. At the end stage of renal failure, kidney shrink, vitamin D activation becomes difficult, and the low calcium blood syndrome appears. The calcification of tuberculoma is absorbed, soft tuberculoma becomes baring, the caseation abscess melts, and the endogenous infection occurs. The cell immunity has decreased, and tuberculosis attacks. It might be such circumstances that tuberculosis happen frequently at the dialysis introduction period.

There are a lot of cases that the caseation necrosis is a little, and the formation of tuberculoma is bad in the pathology opinion. Due to the decrease in the cell immunity, cavities are not formed easily. It is easy to stay in the leaching lesion so that anti-tuberculosis drugs are much effective, and the patients recover easily. However, if the treatment is delayed, it is fatally because hematogenous metastasis are easy to occur and become miliary tuberculosis.

4. AIDS and tuberculosis : Hideaki NAGAI (Department of Respiratory Diseases, National Tokyo Hospital)

With AIDS patients with tuberculosis, there are the following problems on the treatment.

(1) The adverse reactions by antituberculosis drugs tend to occur in AIDS patients. Eleven of 33 AIDS patients with tuberculosis had the adverse reactions (skin rash, fever, liver dysfunction) considered to be due to antituberculosis drugs. It is a very large burden for the HIV infected persons to take simultaneously antituberculosis drugs, medicines for opportunistic infections, and anti-HIV medicines. Since many medicines are taken, it is difficult to determine which drug is the cause once an adverse reaction occurs and all medicines should be often stopped.

(2) The combined use with rifampicin (RFP) is difficult for the protease inhibitors and nonnuclear acid reverse transcriptase inhibitors. RFP induces cytochrome P-450 in liver, accelerates the metabolism of some concomitant drug agents, and reduces blood concentration them remarkably. When starting the two above-mentioned medicines during tuberculosis treatment, RFP should be changed to rifabutin (RFB) which has less induction of P-450 than RFP. However, some procedures are required for acquisition of RFB and it is a little complicated in Japan. CDC mentioned the combined use with RFP and efavirenz (EFV) is possible. So, the treatment with EFV and RFP is recently chosen. However, the monitor of the blood concentration of EFV is required, and the dose of EFV should be increased if it is a low value.

(3) When a highly active antiretroviral therapy (HAART) is given to AIDS patients with tuberculosis, transient worsening of tuberculosis may develop after about two weeks. Cell immunity is recovered by HAART, and this reaction is supposed to be due to the increased response to tubercle bacillus and is called immune reconstitution syndrome.

By the above-mentioned points it is difficult to determine when HAART will be initiated. If it's possible, HAART will not be performed during tuberculosis treatment, and it will be started after the end of tuberculosis treatment. HAART should be started two months after the initiation of tuberculosis treatment in the cases with less cell immunity. However, the start time of HAART should be decided for each case, and it is thought that more cases are still required to know the suitable initiating time.

5. The actual situation and countermeasures of tuberculosis

occurrence in senior citizen (especially, tenants in welfare facilities for elderly people) : Kazutoshi MATSUMOTO (Health Promotion Division, Department of Health and Public Welfare, Aichi Prefecture Government)

To contribute to preventive measures of a mass outbreak of tuberculosis in welfare facilities for elderly people, the actual situation of tenants' health care and tuberculosis occurrence were investigated. And, senior citizen's easiness for tuberculosis infection and tuberculosis measures in the future were considered.

Investigation object by the mailing method were all the special elderly nursing homes, nursing homes, and low cost nursing homes in Aichi Prefecture except Nagoya City. The investigation time was at October 1, 2002. And, its result was compared with a similar investigation executed in 1999.

Investigation vote was collected from all the object facilities 180 (special elderly nursing homes 91, nursing homes 25, and low cost nursing homes 64) in total in number of facilities. As a whole they were 11,674 people, and ratio of 85 years old or more was 40.4%, and ratio of woman who occupied it to tenants was 77.5%.

The consultation rate of recent X-rays of chest inspection was low in the bedridden person of special elderly nursing homes with 86.5% . However, 25.0% has been improved compared with the investigation result in 1999.

There was a tuberculosis occurrence of 64 from 1997 to 2002 years in the entire welfare facilities for elderly people. If the expected value of the tuberculosis occurrence is calculated from the tuberculosis morbidity rate and the number of tenants by sex, age class of Aichi Prefecture in 2002, it becomes 12.2. That of the investigation result in 1999 was 13.6. Both numbers of occurrence actual were less than that of the expected value.

As numbers of occurrence actual were less than that of the expected value, senior citizen's easiness for tuberculosis infection was not proven.

However, as for senior citizen's tuberculosis morbidity rate is strengthening and the ratio of the senior citizen who occupies it is increasing every year, strengthening for the senior citizen tuberculosis measures is hoped. It is necessary to cooperate usually intimately with facilities as measures of the administration through execution and the dissemination etc. of the sanitary education. Aichi Prefecture introduced the medical examination car, which puts the portable X-ray device taking a picture as a bedridden person measures in 2000 fiscal year, and "Tuberculosis measures manual in the senior citizen facilities" was made, and the training association to the senior citizen facilities staff etc. was held.

Key words: Tuberculosis, Diabetes mellitus, Gastrectomy, Dialysis, AIDS, Elderly people

[1]Department of Respiratory Diseases, National Chiba-Higashi Hospital, [2]Division of Respiratory Medicine, Department of Medicine, Nagoya University Graduate School of Medicine

Correspondence to: Fumio Yamagishi, Department of Respiratory Diseases, National Chiba-Higashi Hospital, 673, Nitona-cho, Chuo-ku, Chiba-shi, Chiba 260−8712 Japan.
(E-mail: yamagisf@chibae.hosp.go.jp)