Original Article

PATHOGENESIS OF CHRONIC DISSEMINATED ACINAR PULMONARY TUBERCULOSIS: OKA'S CLASSIFICATION OF PULMONARY TUBERCULOSIS TYPE IIB

— A Discussion through an Analysis of Two Typical Cases —

Hitoshi TOKUDA

Abstract [Purpose] To elucidate the pathogenesis of chronic disseminated acinar pulmonary tuberculosis (Oka's classification type IIB)

[Subjects and Methods] The subjects are two cases of chronic disseminated acinar pulmonary tuberculosis. The pathogenesis were discussed through an analysis of their radiologic findings on admission and in the past.

[Results] Case 1 is a 36 year-old woman whose complaint was slight fever and cervical lymphadenopathy for past four months. Disseminated granular shadows were observed in both lung fields on the chest X-ray on admission. The CT examination indicated that each granule was composed of circumscribed lesion within terminal or respiratory bronchiole, so called acinar lesion. It is compatible with pulmonary tuberculosis type IIB according to Oka's classification. The bronchial lavage yielded *Mycobacterium tuberculosis*. When compared the chest X-ray with that at 4 months before, it is suggested that the granular lesions were first spread hematogeneously and each granule thereafter ruptured into the airway.

Case 2 is a 90 year-old man with slight fever and weight loss. The chest X-ray showed diffuse granular shadows. The CT examination indicated that the lung shadows were composed of disseminated acinar lesions. The diagnosis of tuberculosis was established by a bronchoscopic examination. Comparison of the chest X-ray findings between those at 3 years 9 months before and 8 months before suggests the bronchogenic development of the disease.

[Conclusion] Through an analysis of these two cases, two kinds of pathogenesis were suggested in chronic disseminated acinar pulmonary tuberculosis; namely, one is hematogeneous route and the other is in bronchogenic route.

Key words: Oka's classification of pulmonary tuberculosis type IIB, Chronic disseminated acinar pulmonary tuberculosis, Miliary tuberculosis

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Original Article

ANALYSIS OF TUBERCULOSIS INFECTION AMONG FOREIGNERS USING QuantiFERON®TB-2G TEST

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Abstract [Objective] The purpose of this study was to investigate contacts of a tuberculosis patient among foreigners using QuantiFERON®TB-2G (QFT-2G) test.

[Subjects and Methods] Three index cases in this study were all foreigners. Contacts, who were mostly foreigners and some Japanese, were investigated by a chest X-ray examination, tuberculin skin test (TST) and QFT-2G, and all data were compared.

[Results] Among 48 subjects (30 Vietnamese and 18 Japanese) in case 1, 8 Vietnamese and 2 Japanese were QFT-2G positive. One contacts among 3 most close contacts who lived in the same room with the index case was QFT-2G positive. In case 2, three Chinese among 22 contacts were QFT-2G positive, and a very close contact who lived in the next door to the index case was QFT-2G negative. Seven QFT-2G positive Chinese were identified among 24 contacts in case 3. However, four very close contacts among them were QFT-2G negative.

[Conclusion] Although it was unclear whether QFT-2G positives in cases 1 and 2 were infected with *M. tuberculosis* through the index cases, it is possible to speculate that these QFT-2G positives were already infected with *M. tuberculosis* while they live in their own country based on the prevalence of TB in their countries and the fact that many very close contacts were QFT-2G negative. Also, it was suggested that QFT-2G positives in case 3 may not be infected through the index case, but infected in their country, since all close contacts were QFT-2G negative. The results of this study suggested that using the QFT-2G test for foreigners prior to or soon after their entry to Japan and recommending chemoprophylaxis for those who are QFT-2G positive would be a very efficient control measures against immigrant foreigners with TB infection.

Key words: Foreigners, Tuberculosis outbreak, Tuberculin skin test, QuantiFERON®TB-2G, Prophylaxis

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Original Article

BONE AND JOINT TUBERCULOSIS CONCURRENT WITH TUBERCULOSIS OF OTHER ORGANS

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Abstract [Objectives] To study the characteristics of bone or joint tuberculosis (TB) accompanied by TB in other organs (especially the lung), and to study patients' and doctors' delay in detecting bone or joint TB.

[Subjects and Methods] A retrospective study was conducted on 33 patients with bone or joint TB concurrent with TB of other organs, especially the lung, who were admitted to our hospital between 1981 and 2005. The patients were divided into the following three groups according to the organ of concurrent TB : (1) miliary TB group (N＝10), (2) pulmonary TB group (N＝19), and (3) other TB site group (N＝4). The relationship between bone/joint TB and TB of other organs was studied by comparing the three groups with respect to the time of appearance of musculo-skeletal symptoms or signs such as swelling and pain and that of symptoms or signs originating from other organs, such as cough, sputum, miliary pattern on chest radiograph and superficial lymph node swelling.

[Results] The mean age (SD) of patients was 50.5 (18.9) yr, and the male to female ratio was 23 : 10. Among 33 patients, bone TB (including 18 spinal TB) was detected in 24 patients, joint TB in 14, and abscess in 3 (concurrent lesions in some patients). The mean intervals from onset of symptoms to consultation (patients' delay), from consultation to diagnosis (doctors' delay) and from symptom onset to diagnosis (total delay) were 5.5 (13.9), 3.4 (5.2) and 8.9 (13.9) months, respectively.

(1) Bone/joint TB concurrent with miliary TB (N＝10)

In 8 patients with mean age of 61.0 (17.4) yr, musculo-skeletal symptoms/signs preceded respiratory symptoms or appearance of miliary pattern on chest radiograph by 7.8 (7.2) (range; 1−24) months. The patients', doctors' and total delays were 0.4 (0.5), 7.3 (7.8), and 7.7 (7.6) months, respectively. In most cases, bone/joint TB was diagnosed after the onset of miliary pattern on chest radiograph. In one patient with simultaneous onset of musculo-skeletal and respiratory symptoms/signs (age 21 yr), the interval of total delay was 1 month, and in one patient with musculoskeletal symptoms which appeared six months later than respiratory symptoms (age 28 yr), the interval of total delay was 2 months.

(2) Bone/joint TB concurrent with active pulmonary TB (N＝19)

In this group, the mean age was 52.2 (17.1) yr, and males were predominant (M/F＝15/4). Active pulmonary TB was diagnosed by positive sputum culture in 13 patients, by positive sputum smear or PCR results in 4 patients, and by the clinical course in 2 patients. Ten patients (53％) had a previous TB history. Cavitary lesion was observed in 15 patients, and the upper lobes were predominantly involved on chest radiograph in 19 patients, indicating that the pulmonary TB was probably post-primary (reactivation) in all patients. In 9 patients with mean age of 49.7 (15.7) yr, musculo-skeletal symptoms/signs preceded respiratory symptoms by 14.1 (14.0) (range; 4−48) months. The patients', doctors' and total delays were 13.3 (17.8), 3.8 (6.6), and 17.1 (16.1) months, respectively. On the other hand, in 10 patients with mean age of 54.5 (18.7) yr, musculo-skeletal symptoms/signs and respiratory symptoms/signs appeared simultaneously, and the total delay was 2.7 (1.9) months. Twelve of 19 patients (63％) had complications such as diabetes mellitus, steroid use, and liver diseases.

In cases with miliary or pulmonary tuberculosis, the total delay in diagnosis (Y) correlates positively with the time lag from onset of musculo-skeletal symptoms to respiratory symptoms/signs (X), and the regression line ($Y＝0.94X＋2.3$, $r＝0.98$, $p＜0.001$) was almost linear ($Y＝X$), indicating that the diagnosis of bone/joint TB was made just after the diagnosis of miliary or pulmonary TB.

(3) Bone/joint TB concurrent with TB of other sites (N＝4)

In 2 female cases (21 and 28 yrs) with cervical lymph node TB, musculo-skeletal symptoms/signs and cervical lymph node swelling appeared simultaneously. In a 54-yr male patient, musculo-skeletal symptoms/signs appeared 5 years after appearance of testicular enlargement, and testicular TB was diagnosed by biopsy simultaneously. In a 33 year-old male patient, musculo-skeletal symptoms/signs appeared 7 months after the drainage of pleural and pericardial effusions (TB was not diagnosed initially), and then the diagnosis of bone/joint, pleural, and pericardial tuberculosis was made for the first time.

[Conclusions] In middle-aged or elderly patients with active bone/joint TB, miliary TB is sometimes caused by bacillemia originating from the infected bone/joint lesions. In cases with bone/joint TB and concurrent pulmonary TB, bone/joint TB and pulmonary TB are probably reactivated independently as a result of decreased systemic immunocompetence.

Key words: Bone and joint tuberculosis, Miliary, Pulmonary, Delay, Reactivation

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—————— Original Article ——————

MOLECULAR EPIDEMIOLOGY OF *MYCOBACTERIUM TUBERCULOSIS*
— Comparison between Multidrug-Resistant Strains and Susceptible Strains —

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Abstract [Purpose] Comparing multidrug-resistant *M. tuberculosis* strains with susceptible strains by molecular epidemiological methods.

[Methods] We examined 109 multidrug-resistant strains (MDR-TB) and 226 susceptible strains (S-TB) derived from National Hospital Organization Kinki-chuo Chest Medical Center by restriction fragment length polymorphism (RFLP) with IS*6110*, and Spacer oligonucleotide typing (Spoligotyping).

[Results] In the case of MDR-TB, 47 strains (43.1%) belonged to 12 descriptions of clusters and the number of IS *6110* copies per isolate ranged from 9 to 25. Similarly, 99 strains (43.8%) belonged to 20 descriptions of clusters in S-TB and the distribution of IS *6110* copies were from 1 to 20. On the other hand, 84 strains of MDR-TB (77.1%) and 191 strains of S-TB (84.5%) belonged to Beijing family by Spoligotyping.

[Conclusion] MDR and susceptible *M. tuberculosis* strains were characterized similarities in ratio of clusters by RFLP patterns and high proportion of Beijing family by Spoligotyping. These finding supported the possibility that infectiousness of MDR-TB might be similar to that of S-TB.

Key words: *M. tuberculosis*, IS*6110*-RFLP, Spoligotyping, Multidrug-resistant, Susceptible

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Review Article

MYCOBACTERIOSIS AS ZOONOTIC DISEASE
— Comparative Pathological Study on *Mycobacterium avium* Complex Infection —

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Abstract *Mycobacterium avium* complex (MAC) infection has been giving major impact on human health. MAC infection is also one of zoonosis transmittable from environmental reservoirs to domestic animal such as pig, and from wildlife to human. Although the relationship between pig MAC infection and human MAC infection has been suggested, it has not been clarified about difference of pathogens, differences in the pathogenesis of the disease, and differences in pathological findings between them. As one of zoonosis, hog farms suffer from the epidemic in pig population and it may causes huge economical loss. At the same time, from pig to human transmission of MAC has been worried. Therefore, the control of MAC infection among hog farms is a very important issue both for pig industries and for human public health. We have demonstrated that the specific MAC strains can spread through pig market in the main island of Okinawa. In pig MAC infection, pathogens are infected orally, and granulomatous lesions are formed in abdominal lymph nodes. Subsequently, it spreads lymphogenously or hematogenously and forms disseminated disease. Pathologically, calcified lesion was formed within several months. These findings are quite different from human MAC disease, in which the infection was caused by inhalation, and form granulomatous lesions in lungs, and rarely cause lymph node swellings. Since the pathogenesis of human MAC respiratory infection has not been well clarified, it may be very important to examine the mechanism of pig MAC infection to find out some clues to explain the mechanism of human MAC infection.

Key words: Zoonosis, *Mycobacterium avium* complex, Pig, Pathology, Granuloma

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