Original Article

CLINICAL ANALYSIS OF EXTENSIVELY-DRUG RESISTANT TUBERCULOSIS (XDR-TB) IN OUR HOSPITAL

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Abstract [Objective] We analyzed the clinical characteristics of extensively-drug resistant tuberculosis (XDR-TB).

[Materials and Methods] Thirteen cases diagnosed with XDR-TB encountered in our hospital over the last ten years were enrolled in our study.

[Results] The patients included 9 males and 4 females. The mean age was 49.1 years old in males and 42.0 years old in females. Eight patients were Japanese and 5 were foreigners (Chinese, 3; Korean, 1; Nepali, 1). Nine cases had a smoking history and 6 had underlying diseases, including 1 with bacterial pneumonia, 3 with diabetes mellitus, 1 with chronic renal failure, and 1 with collagen vascular disease receiving immunosuppressive treatment. All 13 cases had been diagnosed at other hospitals. The mean period from TB diagnosis to XDR-TB diagnosis was 56.8 months, and the mean period from TB diagnosis to referral to our hospital was 81.6 months.

Among the 13 cases, 3 had no drug sensitivity, 1 was sensitive to only 1 drug, 2 were sensitive to 2 drugs, 6 were sensitive to 3 drugs, and 1 was sensitive to 4 drugs. Nine of the 13 cases had surgical treatment. Six cases, all of whom had surgical treatment, showed negative conversion in sputum examinations. Three patients died, including two who had surgical treatment.

Among the 3 cases with no drug sensitivity, 1 was cured after surgical treatment. Another case had been working in the same hospital with two other MDR-TB cases. Two of the three had the same RFLP pattern.

[Conclusion] XDR-TB and MDR-TB are man-made diseases. We need to take measures not to create more XDR strains and induce more MDR-TB cases.

Key words: XDR-TB, Drug sensitivity test, Chemotherapy, Surgical treatment, RFLP (restriction fragment length polymorphism) analysis

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Review Article

A NEW ANTI-MYCOBACTERIAL AGENT, RIFABUTIN

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Abstract This is a review of non-clinical and clinical study results of rifabutin (Mycobutin®, RBT) which was approved as a new anti-mycobacterial agent 38 years after rifampicin (RFP) was approved in Japan. The anti-bacterial actions of RBT were similar to those of RFP, but its potency was stronger (4 to 32 times in MIC_{90}). RBT showed excellent penetration in cells (9 times in neutrophil, 15 times in monocyte, against plasma concentration) and in tissues (5 to 10 times in pulmonary tissue). Clinical efficacy of RBT (150 mg, as well as 300 mg daily) was comparable to that of RFP 600 mg daily, in the treatment of newly diagnosed tuberculosis, drug-resistant tuberculosis, and the NTM diseases. In addition, RBT 300 mg showed significant prophylactic effect on the development of disseminated MAC infection in HIV positive subjects. Most of the adverse events of RBT were the same as those of RFP, including drug-drug interactions related to the induction of CYP3A4. The concomitant use of RBT (over 450 mg) with clarithromycin induces uveitis, which warrants special attention. It is expected that the efficacy and safety of RBT in Japanese subjects will be evaluated in Japan through the accumulation of clinical experience.

Key words: Rifabutin, Anti-mycobacterial agent, Tuberculosis, Non-tuberculous mycobacteriosis, AIDS, HIV infection

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Short Report

THE CURRENT STATUS OF FLUOROQUINOLONES AND OTHER OFF-LABEL DRUG USE FOR TUBERCULOSIS IN JAPAN

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Abstract [Objectives] To clarify the present state and problems of off-label drug use in tuberculosis treatment in Japan.

[Materials and Methods] Questionnaire survey by mail to 252 hospitals with tuberculosis wards.

[Result] It was found that 146 out of 160 hospitals returning the questionnaire had active tuberculosis ward(s). Fluoroquinolones(FQs) were being used in 119 (81.5%) hospitals, of which 115 used levofloxacin. The reasons for using FQs were : i) adverse reactions to other antituberculosis drug(s) in 97 hospitals, and ii) drug-resistance in 80 hospitals. The perceived problems in using FQs were : i) its use for tuberculosis is not approved (often not reimbursed by medical insurance), cited by 73 hospitals ; ii) increased out-of-pocket medical fees for patients (not covered by public service), cited by 48 hospitals; iii) official compensation for severe adverse reactions cannot be guaranteed for off-label use, cited by 19 hospitals. Other off-label drugs such as linezolid are also used in 37 hospitals.

[Discussion] Fluoroquinolones, especially levofloxacin, are widely used in tuberculosis treatment in Japan for patients with adverse reactions and/or dug-resistance to other antituberculosis drugs. As these drugs have not yet been approved for tuberculosis treatment and therefore are not included in "the Standards of Tuberculosis Treatment" established by the government, the costs for FQs and other off-label drugs are not covered by public subsidies for medical treatment, thus increasing the economic burden for patients, which may in turn cause drop-out, especially in cases of MDR-TB. Further, FQs are not under control of the Tuberculosis Advisory Committee of the Health Center, which has played an important role in ensuring the standard tuberculosis treatment in Japan.

[Conclusion] FQs should be included in the Standards of Tuberculosis Treatment to secure adequate chemotherapy for tuberculosis.

Key words: Indication, Drug-resistant tuberculosis, Fluoroquinolone, Levofloxacin

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