Cardiac Involvement of Relapsing Polychondritis in Japan;

An Epidemiological Study

by

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Short running footline: Cardiac involvement of RP in Japan

Relapsing polychondritis (RP) is a relatively rare disease, exhibiting swelling of the ear, destruction of the nose, fever, and arthritis often accompanying autoimmune reactions [1]. Tracheobroncheal involvement was potentially lethal through the occlusion [2]. Cardiac complications of RP begin to attract increasing attention because it is the second most frequent cause of mortality in this disease [3, 4, 5].

We conducted large scale epidemiological study in Japan [2] and revealed the high mortality rate in RP patients with cardiac involvement. We reanalyzed the data in view of cardiac involvement in patients with RP.

A Multi-institutional study survey of Japanese major medical facilities was conducted from July to December 2009 [2, 6]. All subjects being sent the questionnaire were informed of the purpose of the study and the responses would be kept confidential. All the authors reviewed the questionnaire.

We obtained responses from 121 facilities and clinical information of 239 RP patients was accumulated. The average age of onset diagnosis was 52.7 years old (range, 3~97) and the male-to-female ratio was 1.1:1 (127 males, 112 females) [2].

Biopsies were performed in 228 patients (95.4 %) and histological confirmation of RP was obtained in 138 patients (57.7 %). Auricular and nasal chondritis were shown in 187 patients (78.2%) and 94 patients (39.3 %), respectively, during follow-up. One hundred and twenty patients (50 %) showed airway involvement. Forty nine patients (20.5 %) suffered from upper airway collapse and 42 patients (17.6 %) underwent tracheotomy.

Among 239 RP patients, 17 cases (7.1 %) developed cardiac

involvement. Mean age of onset of RP with cardiac involvement was 64.6 years old, suggesting that cardiac involvement developed later than other patient group. The ratio of men to women was 3.25 to 1 and thus men predominantly developed cardiac symptoms. RP patients with cardiac involvement were diagnosed with the diagnostic criterion [7], accompanying the histological confirmation (all, auricular chondritis) in 8 patients (53 % of the 15 patients who had histological examinations). When cardiovascular symptom is the first symptom appeared in the RP patients, even though such patients are not prevalent, it is hard to reach final diagnosis of RP. Thus, it is possible that prevalent rate of cardiovascular symptoms is underestimated in Japan. In the literatures, cardiac involvement was reported to be 6 to 23 % in patients with RP, almost comparable with that of Japan [5].

Differential diagnosis of cardiovascular complications of RP, from such symptoms of atherosclerosis/aging origin was not completely clear from this type of epidemiological studies.

Japanese RP patients developed myocardial infarction/angina pectoris (5 cases out of 239 cases, 2.1 %), valvular heart disease (5 cases, 2.1 %; mitral regurgitation (MR) 3 cases; aortic regurgitation (AR) 2 cases) and aortic aneurysm/aortitis (3 cases, 1.7 %). It has been reported that MR and AR—attributable to progressive dilation of the aortic root of the ascending aorta rather than to inflammation of the valve leaflet—occur in about 2–6% of the patients [5, 8]. 2.1 % of the patients showed coronary artery diseases in this Japanese study. The underlying mechanism is uncertain, although vasculitis may account for a few cases.

Our survey revealed that RP death rate in Japan was 9 % [2]. When we focused on RP with cardiac involvement, 6 cases had died out of 17 cases; accordingly the death rate was 35 %. Three deaths were caused by valvular heart disease. The remaining two patients were myocardial infarction and severe cardiac failure. A patient died suddenly from uncertain causes. Even though complete heart block, aortic valve rupture and acute aortic insufficiency have been reported as fatal cardiovascular complications [5, 8], we did not obtain such information in this Japanese study.

In order to make more accurate and easier diagnosis of RP, we have to establish assay systems which measure RP specific and RP associated disease markers. We are going to study whether serum soluble triggering receptor expressed on myeloid cells 1 (sTREM1) levels become one of RP associated markers [9].

Further studies are needed to disclose the entire clinical pictures of RP patients with cardiac involvement [10]. In addition, conventional treatment, such as steroid and immunosuppressant, which had been administered on a vast majority of the patients, was not fully satisfactory. Establishment of a new therapeutic strategy for cardiac symptoms in patients with RP is awaited.

In conclusion, 7.1 % of Japanese patients with RP developed relatively severe cardiac involvement and cardiac involvement appeared to be a major determinant of disease severity in patients with RP in Japan as well.

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