The occurrence of Japanese cedar pollinosis with rheumatoid arthritis

Sirs,

Rheumatoid arthritis (RA) is a systemic disease characterized by a chronic joint inflammation that leads to destructive lesions of joint cartilage and periarticular bone. Immune responses are regulated by two subtypes of $CD4^+$ T helper (Th) cells, designated Th1 and Th2. RA has been recognized as a Th-1 dominant disease, whereas atopic allergy has been recognized as a Th-2 dominant disease. Therefore, a functional dichotomy between Th1-dominated immune reactions in RA and Th2-mediated immune reactions typical of atopic allergy, including Japanese cedar pollinosis (JCP), has been suggested (1-7). To investigate the occurrence of a case history of allergy in RA patients and to compare the disease activity of RA between RA patients with allergic diseases and those without allergic diseases, we conducted a large observational cohort study of RA patients (The 6th Japanese version of the IORRA study (Institute Of Rheumatology, Rheumatoid Arthritis)). The subjects were 4578 outpatients (782 men and 3796 women and the average age was 58.2 years) diagnosed with RA (8). All individuals were assessed by a physician-administered questionnaire for a medical history of pollinosis, rhinitis, bronchial asthma, atopic dermatitis, urticaria, and drug allergy. Furthermore, patients were asked about symptoms such as nasal symptoms and eye symptoms, as well as the duration of these manifestations and the diagnosis of JCP was made. As for the disease severity of RA, subsets of American College of Rheumatology (ACR) core set were used, i.e. the number of tenderness or swelling joints, visual analog scale (VAS) score, Health Assessment Questionnaire (HAQ) Japanese version of the HAQ (J-HAQ) score (9), and C-reactive protein (CRP). For statistical analysis we introduced two methods, the *recursive partitioning and regression tree* (rpart) model (10) and the *generalized linear model* (GLM).

We observed almost identical occurrence of allergies in RA patients to that in the general Japanese population (pollinosis 37.6%, JCP 19.3%, bronchial asthma 6.3%). We investigated whether RA was less severe in patients with JCP than in patients without it. When considering medication, the non-allergic group were prescribed more PSL and less DMARDs than the JCP group and there is a possibility that anti-inflammatory effect of PSL affects not only the disease activity of RA, but also the symptoms of JCP, resulting in the masking of JCP symptoms (Fig. 1A). To clarify this issue, we divided the cohort into 3 groups according to PSL dosage for the treatment of their RA as follows (A); those who took more than 5mg/day of PSL, (B); those who took less than 5mg/day of PSL, (C); those who received no PSL (Fig. 1B). In the A group,

A

Variables	JCP (n=880)	Non-allergy (n=1627)	P-value
Men/Women	109/771	335/1292	P<0.001
Side effect in the past 6 month (yes/no/unknown)	253/390/157	321/783/523	P<0.001
Current Medication (PSL/DMARD/none)	381/363/136	849/589/189	P<0.001
Age(yr)± SD	53.5± 11.3	60.6± 12.8	P<0.001
Age at onset(yr)± SD	43.4± 12.1	48.6± 14.0	P<0.001
Disease duration(yr)± SD	10.0± 8.0	11.8± 9.2	P<0.001
TJC, SJC(n)± SD	3.2± 5.0, 3.0± 4.4	3.1± 5.2, 3.0± 4.2	p>0.1
VAS(P, G, D) score ± SD	33.3± 27.4, 34.6± 26.2, 16.4± 15.2	32.8± 26.7, 34.4± 26.1, 17.1± 15.6	p>0.1
HAQ, J-HAQ score ± SD	0.6± 0.7, 0.7± 0.7	0. 8± 0.8, 0.8± 0.8	P<0.01
CRP(mg/dl)± SD	1.2± 1.7	1.5± 1.9	P<0.001
ESR(mm/h) ± SD	31.1± 22.1	36.3± 24.6	P<0.001
RF(mg/dl)± SD	136.9± 261.3	172.9± 314.8	P<0.1
Dose of oral PSL(mg/day)± SD	2.3± 2.8	2.8± 3.2	P<0.001

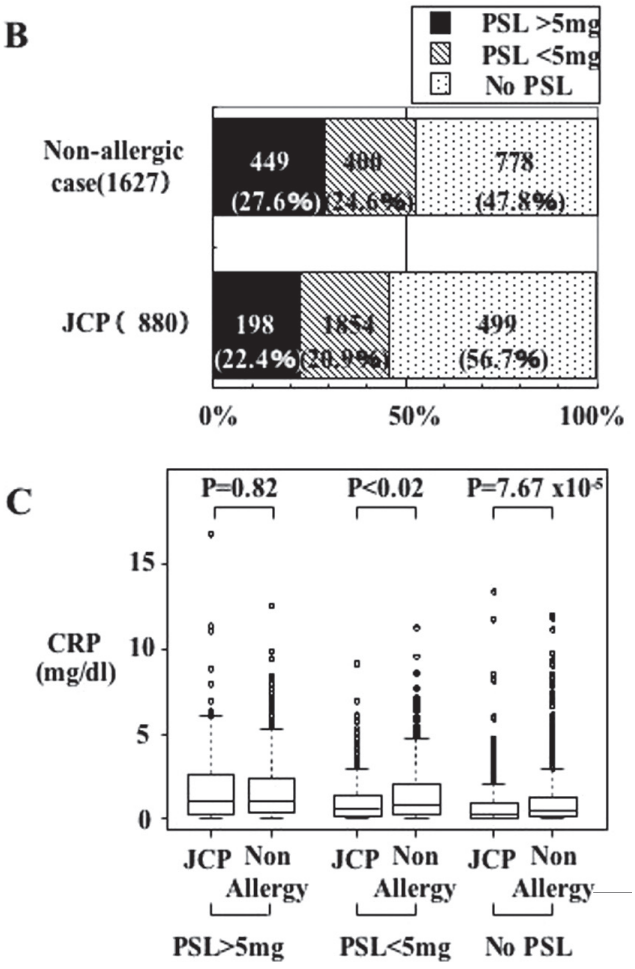

Fig. 1A. Characteristics of JCP group and non-allergic group.

Fig. 1B. Comparison of PSL dosage in JCP and non-allergic cases

(A): those who take more than 5mg/day of PSL, (B): those who take less than 5mg/day of PSL, (C): those who do not take PSL. Both in the (A) and (B) groups, non-allergic cases were higher than JCP cases, and in the (C) group, JCP cases were higher than non-allergic cases.

Fig. 1C. The evaluation of CRP levels among JCP and non-allergic cases according to PSL dosages.

there were no significant differences as to the mean value of CRP, HAQ and J-HAQ scores. On the other hand, both in the B and C groups, the mean value of CRP, HAQ score, J-HAQ score were lower in JCP cases than in non-allergic cases. The mean value of CRP was significantly lower in JCP cases (JCP cases 1.18 and non-allergic cases 1.57 for (B) group (n = 584; Mann-Whitney U test, $p < 0.02$), and JCP cases 0.81 and non-allergic cases 1.14 for (C) group (n = 1277; Mann-Whitney U test, $p < 7.67 \times 10^{-5}$) (Fig. 1C). Most importantly, in group C, which was considered to be not influenced by the anti-inflammatory effect of PSL, there was a dramatic difference in the CRP levels between JCP cases and non-allergic cases.

We concluded that the disease activity of RA has a tendency to be negatively associated with the presence of JCP and speculated that patients with JCP have some genetic predisposition to develop milder RA.

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Erratum corrige

Early onset neutropenia after rituximab in lupus nephritis *R. Enríquez, J. Borrás-Blasco, A.E. Sirvent, M. Masía, F. Amorós* published in *Clin Exp Rheumatol* 2007; 25: 345, was erroneously listed in the Table of Contents with the first author, printed as *E. Enríquez instead of R. Enríquez*. We apologise to Dr. Ricardo Enríquez for this error.