Letters to the Editor

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CD180 (RP105) in rheumatic diseases

Sir, CD180 (RP105) is a leucine-rich repeat (LRR) molecule expressed on the membrane of B-cells [1, 2]. The molecules bearing LRRs control the recognition of pathogens and the subsequent activation of the immune system [3, 4]. CD180 belongs to the toll-like receptor family of pathogen receptors. CD180 takes part in B-cell recognition and lipopolysaccharide signalling [5].

Recent studies have shown decreased CD180 expression on B-cells in systemic lupus erythematosus (SLE) [6]. The loss of CD180 is associated with B-cell activation and increased disease activity in SLE patients. We investigated the expression of CD180 on peripheral blood B-cells in patients with various types of rheumatic disease.

Eighty-six patients with rheumatic diseases, who were receiving prednisolone <15 mg/day, were recruited from our out-patient clinic. Blood samples were obtained from patients with systemic sclerosis (SSc) (n = 21; all females); primary SS (n = 18; all females), angitis syndrome (n = 13; 9 males and 4 females), Behçet’s disease (n = 11; 5 males and 6 females), mixed connective tissue disease (MCTD) (n = 10; all females); polymyositis (PM) (n = 8; 3 males and 5 females)/dermatomyositis (DM) (n = 5; 2 males and 3 females). Thirty-one healthy controls (12 males and 19 females) were also evaluated.

Two-colour flow cytometric analysis was performed using fluorescein isothiocyanate-conjugated anti-human CD180 monoclonal antibody (mAb) MHR-73 (a kind gift from Dr K. Miyake, Saga Medical School, Saga, Japan) and R-phycoerythrin-conjugated anti-human CD19 mAb. The labelled cells were analysed on a FACScan (Becton Dickinson, Mountain View, CA, USA). List mode data were collected and reanalysed using WinMDI (version 2.8) software written by J. Trotter (http://facs.script.edu).

The percentage of CD180-negative B-cells in the healthy subjects [mean ± s.d. (range)] was 2.6 ± 1.5% (0.8–7.3%). The percentages of CD180-negative B-cells varied in patients with rheumatic diseases. The percentages of CD180-negative B-cells in the peripheral blood of patients with SS (14.5 ± 10.3%, 1.4–35.7%) and dermatomyositis (DM) (23.5 ± 13.3%, 2.8–36.5%) were highly increased. The percentages of CD180-negative B-cells in other rheumatic diseases were as follows: SSc (5.4 ± 4.1%, 0.4–14.7%); angitis syndrome (4.7 ± 3.2%, 0.4–11.4%); Behçet’s disease (6.9 ± 5.4%, 0.7–18.0%); MCTD (5.1 ± 3.3%, 0.5–10.3%); polymyositis (PM) (3.5 ± 3.2%, 0.4–9.5%).

The Mann–Whitney U-test was used to determine the statistical significance of differences between groups of diseases. A P value of < 0.05 was considered significant.

The percentages of CD180-negative B-cells in SS (P = 0.00001) and DM (P = 0.0025) were significantly higher than in normal controls. The percentage of CD180-negative B-cells in DM patients was significantly higher than in patients with PM (P = 0.013). Other rheumatic diseases (SSc, P = 0.018; angitis syndrome, P = 0.049; Behçet’s disease, P = 0.02; MCTD, P = 0.036) showed percentages that were not as high as the two diseases (PM and SS) but still significantly higher than in normal subjects. However, the percentage of CD180-negative B-cells in PM was not significantly higher than that in normal subjects.

Recent studies have suggested that the CD180-negative B-cells are activated B-cells [6]. Moreover, it is well known that B-cells in SS patients are in a polyclonally activated state [7]. It is understandable, therefore, that there was a large proportion of CD180-negative B-cells in our SS patients.

Interestingly, the percentage of CD180-negative B-cells was elevated in DM but not in PM. DM is clinically similar to PM (except for the presence of skin manifestations). However, previous reports have suggested that PM and DM are aetiologically different [8–10]. They suggested the involvement of humoral immune mechanisms in DM and cellular immunity in...
PM. The difference between DM and PM in the percentage of CD180-negative B-cells probably reflects a difference in pathophysiology.

We demonstrated that the percentage of CD180-negative B-cells was significantly increased in SS and DM, in which B-cell activation is postulated to be involved. These findings are clinically relevant in the evaluation of rheumatic diseases and in the study of their immunological mechanism.

Furthermore, it is important to investigate correlation between the decreased level of CD180 expression and clinical features, total immunoglobulin (Ig) levels and disease activity, especially in SS and DM. The correlation between the percentage of CD180-negative B-cells and the total Ig level in SS was unclear in the present study. In some patients with DM the number of CD180-negative B-cells appeared to have been associated with disease activity. However, it will be necessary to accumulate cases and investigate the correlation of the activity of disease with CD180 expression on B-cells in SS and DM.


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