S100A11 (calgizzarin) is released by circulating mononuclear cells and its elevated plasma levels distinguish systemic lupus erythematosus patients from healthy individuals

Sirs,

Systemic lupus erythematosus (SLE) is a chronic autoimmune condition with complex immunological pathogenesis and diverse clinical features, as a consequence of multi-system inflammation (1). Although there has been a significant progress in the management of patients with SLE, there is an unmet need for specific diagnostic or predictive biomarkers for routine clinical use. Certain members of S100 protein family such as S100A11 and S100A12 are up-regulated in several autoimmune inflammatory disorders, including SLE (2-4), and their potential as diagnostic or prognostic biomarkers is emerging. S100A11 (calgizzarin) is a less known S100 protein that has been extensively studied in cancer (5). Very recently, our group showed an implication of S100A11 in the pathogenesis of rheumatoid arthritis (RA) and thereby its potential role in autoimmune diseases (6). We described a local accumulation of S100A11 protein in the synovial tissues and fluids of patients with RA and its association with inflammation and disease activity (6). Altogether, these findings prompted our present study focusing on S100A11 in SLE. Plasma was obtained from 44 patients with SLE (44 females; mean age ± SD: 40±16 years), 40 patients with RA (27 females; 13 males; mean age ± SD: 54±11 years), 38 patients with idiopathic inflammatory myopathies (IIM) (28 females; 10 males; mean age ± SD: 53±14 years), 40 patients with systemic sclerosis (SSc) (35 females and 5 males; mean age ± SD: 54±11 years), and 41 healthy controls (HC) (35 females and 6 males; mean age ± SD: 44±11 years). SLE patients fulfilled the revised 1997 American College of Rheumatology classification criteria for SLE (7). Patients with IIM, SSc and RA met their classification criteria (8-11). SLE patients’ disease activity was assessed using the SLEDAI-2K (12). Baseline characteristics of patients with SLE are given in Table 1. Peripheral blood mononuclear cells (PBMCs) were isolated from all participants. Statistical analyses were performed using IBM SPSS v. 22 software (IBM SPSS, Armonk, NY, USA). Data were expressed as median (IQR). Systemic levels of S100A11, alike of other S100 proteins (2-4), were significantly elevated in all SLE patients in contrast to HC (7.2 [2.9; 16.6] vs. 2.4 [1.5; 9.9], p<0.0001) (Fig. 1A). When compared to other systemic rheumatic diseases, circulating S100A11 was higher in SLE patients in contrast to patients with IIM (p<0.0001), SSc (p<0.0001) or RA (p=0.01) (Fig. 1A). No difference between the SLE patients with low disease ac-
tivity (SLEDAI <6; n=35) and high disease activity (SLEDAI ≥6; n=9) was observed (6.9 [2.4; 18.8] vs. 8.7 [2.9; 16.6], p=0.709).

Of interest, we found no significant association of circulating S100A11 with laboratory parameters and clinical manifestations of SLE, although it slightly correlated with accumulated damage/organ failure over time (Table I). This is in line with our findings of the SLEDAI activity (SLEDAI <6; n=35) and high disease activity (SLEDAI ≥6; n=9) was observed (6.9 [2.4; 18.8] vs. 8.7 [2.9; 16.6], p=0.709).

The increase of S100A11 in plasma of patients with SLE, probably due to the low mean age of the SLE patients. In conclusion, elevated levels of S100A11 in plasma of patients with SLE, probably due to the low mean age of the SLE patients.

Figure 2. Expression and release of S100A11 by PBMCs.

Expression of S100A11 mRNA in PBMCs from patients with SLE and HC (A). PBMCs from SLE patients spontaneously release significantly higher levels of S100A11 compared to the cells from HC (B). The horizontal bar represents mean.

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