Serum aminoacyl-tRNA synthetase-interacting multifunctional protein-1 (AIMP1), a novel disease activity predictive biomarker of systemic lupus erythematosus

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Abstract

Objective

Secreted aminoacyl-tRNA synthetase-interacting multifunctional protein-1 (AIMP1) has been reported to have pro-inflammatory properties. The aim of this study was to evaluate the clinical significance of serum AIMP1 in patients with systemic lupus erythematosus (SLE).

Methods

Serum levels of AIMP1 were measured in 160 patients with SLE using a human AIMP1 ELISA kit. Eighty patients were classified as active SLE (SLEDAI-2K ≥ 5), and 80 patients were classified as stable SLE. Correlation between serum AIMP1, SLE disease activity index-2000 (SLEDAI-2K), and laboratory variables related to disease activity or inflammatory burdens were assessed using Pearson's correlation analysis. The optimal cut-off value for serum AIMP1 to predict active SLE was estimated by using a receiver operator characteristic curve, and logistic regression analysis was used to compare the odds ratios (ORs) of laboratory variables in predicting active SLE.

Results

The median serum AIMP1 was higher in patients with active SLE than those with stable SLE (8.0 vs. 6.5 ng/ml, p<0.001). Serum AIMP1 demonstrated correlation with SLEDAI-2K and laboratory variables related to disease activity or inflammatory burdens. The optimal cut-off AIMP1 to predict active SLE was 10.09. Multivariate logistic regression analysis including conventional laboratory variables demonstrated that serum AIMP1 ≥10.09 ng/ml (OR 3.919, 95% confidence interval 1.223–12.564, p=0.022) was useful in predicting active SLE.

Conclusion

Serum levels of AIMP1 were associated with disease activity of SLE and could predict active SLE based on SLEDAI-2K.

Key words

aminoacyl-tRNA synthetase-interacting multifunctional protein-1, systemic lupus erythematosus, disease activity, inflammation

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Introduction

Systemic lupus erythematosus (SLE) is a prototypical systemic autoimmune disease characterised by excessive autoantibody production and immune complex formation in its pathophysiology (1). Various autoreactive immune cells have been discovered to contribute to the development and exacerbation of SLE (2-4). Among them, dendritic cells and B cells remain at the forefront of the pathogenesis of SLE, promoting the production of interferon-α and autoantibodies (3, 5). Additionally, autoreactive immune cells can activate nuclear factor kappa B (NF-κB) (6) via extracellular signal-regulated kinase (ERK)/mitogen-activated protein kinase (MAPK) pathways (7, 8). Activated NF-κB, in turn, induces the expression of its downstream genes including interferon-γ, interleukin (IL)-1, IL-2, IL-6, IL-12, IL-17 and tumour necrosis factor (TNF)-α (9-11). In addition, SLE may be affected by the alteration in T cell population such as decreased Treg cells and increased Th17 cells and follicular helper T cells (12). Therefore, identifying a molecule to reflect the dysregulation of autoreactive immune cells and imbalance of cytokines in the blood of SLE patients would be a feasible biomarker to predict disease activity of SLE.

Transfer ribonucleic acids (tRNAs) generally consist of 75–95 nucleotides (13) and play pivotal roles in the process of protein translation by carrying specific amino acids to the ribosomes based on the codons of messenger RNA (14). So far, 20 different tRNAs have been discovered in humans and each amino acid is charged with a cognate tRNA via aminoacyl-tRNA synthetases (ARSs) (15). Compared to prokaryotic ARSs, ARSs in mammals form a multi-tRNA synthetase complex, including 11 different ARSs and three non-enzymatic factors such as aminoacyl-tRNA synthetase-interacting multifunctional protein (AIMP)1/p43, AIMP2/p38 and AIMP3/p18 (16). Several lines of evidence suggest that AIMPs appear to participate in the assembly of the complex-forming enzymes: 1) AIMPs are tightly linked with each other, resulting in the interplay of the intracellular stability of each AIMP; 2) each AIMP has its preferred interacting enzymes; and 3) AIMP1, especially, seems to be a crucial cofactor because of its centric localisation in the multi-tRNA synthetase complex, which suggests that it may facilitate the delivery of tRNAs to the catalytic sites of bound ARSs (17).

Apart from the function of AIMP1 bound to the multi-tRNA synthetase complex, AIMP1 could be secreted into the circulatory system upon hypoxia and apoptotic/necrotic cell death and it may have several immune-stimulatory effects (18): first, secretory AIMP1 may promote angiogenesis by ERKs activation (19); second, AIMP1 may stimulate monocytes and macrophages to produce pro-inflammatory cytokines such as TNF-α, IL-6, IL-8 and macrophage chemotactic protein (MCP)-1 via p38 MAPK and NF-κB (20); third, AIMP1 may induce dendritic cell maturation and increase IL-6 and IL-12 production (21). In addition, we previously demonstrated that serum AIMP1 levels were higher in rheumatoid arthritis patients than healthy controls and a monoclonal antibody targeting AIMP1 significantly ameliorated the severity of arthritis and reduced serum IL-1β, IL-8, MCP-1 and TNF-α levels in mice with collagen induced arthritis (22).

Given that there could be a link between the pathogenesis of SLE and the extended role of secretory AIMP1, it could be reasonably speculated that AIMP1 might participate in the pathophysiology of SLE. However, there has been no report regarding the role of AIMP1 in SLE to date. Hence, in the present study, we investigated whether serum AIMP1 is associated with disease activity of SLE and whether it can predict active SLE based on SLE disease activity index (SLEDAI)-2K (23).

Materials and methods

Patients

We reviewed the medical records of 160 patients with SLE who had been diagnosed at the Division of Rheumatology, Yonsei University College of Medicine, Severance Hospital and who provided blood for serum storage from March 2015 to September 2016. The inclusion criteria were as follows: 1) patients who fulfilled the 1997 revised American College of Rheumatology classification cri-

teria for SLE (24); 2) those who had no medical conditions, such as malignancies, infectious diseases, and autoimmune diseases other than SLE, influencing serum AIMP1, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) (25, 26); 3) those who had well-described medical documents regarding both clinical and laboratory items of SLEDAI-2K assessed and measured on the same day of serum storage; and 4) those who had laboratory results related to inflammatory burdens other than SLEDA1-2K measured on the same day of serum storage. Serum samples of healthy control volunteers (n=43) were obtained from after informed consent was obtained at the Severance Hospital Health Centre. This study was approved by the Institutional Review Board of Severance Hospital and conducted in accordance with the principles set forth in the Declaration of Helsinki.

Clinical and laboratory data and medications

Demographic data included age, gender, and disease duration. SLEDAI-2K was used as an index for disease activity of SLE and was calculated using clinical features and laboratory data such as anti-ds DNA, complement (C)3, C4 and counts of white blood cells (WBCs), lymphocytes and platelets and haemoglobin on the same day as serum storage. Additionally, we reviewed laboratory data other than those required for SLEDAI-2K reflecting the inflammatory burden of SLE such as ESR and CRP. We set the cut-off for SLEDAI-2K at 5 to divide active and stable SLE, and active SLE was defined when patients had a sum of SLEDAI-2K scores of ≥ 5 (27). Patients were defined as having disease remission when they had SLEDAI-2K score of 0 and without glucocorticoid treatment (28). All laboratory data were obtained on the same day of serum storage. Medications were identified using the Korean Drug Utilization Review system and only medications that were currently being administered were counted.

Measurement of serum AIMP1

We measured serum AIMP1 level using stored serum samples of SLE patients and healthy controls. Human AIMP1 ELISA kits were purchased from Cloud-Clone Corp. (Houston, TX, USA), and AIMP1 levels were measured according to the manufacturer's instructions. Briefly, each sample was diluted with PBS at a ratio of 1:5, 100 μl was added to each well, and the plate covered with plate sealer and incubated for 1 h at 37°C. Then, 100 μl of detection reagent A working solution was added to each well, the plate was covered with the plate sealer, and the plate was incubated for 1 h at 37°C. Each well was washed three times with 350 μl of washing solution. Working solution of detection reagent B (100 μl) was added to each well, the plate was covered with the plate sealer, and the plate was incubated for 30 min at 37°C. The plate was then washed five times with washing buffer. Subsequently, 100 ml of 3, 3', 5, 5' - tetramethylbenzidine (TMB) substrate solution was added to each well and the plate was incubated 15 min at room temperature in the dark. Then, 50 μl of Stop solution (0.1 N sulfuric acid) was added to each well, and the O.D. value of each well was measured at 450 nm.

Statistical analyses

Continuous variables are presented as medians with inter-quartile ranges (IQR), and categorical variables are expressed as frequencies and percentages. Continuous variables were compared using the Student's *t*-test or the Mann-Whitney *U*-test, and categorical data were compared using the Chi-squared test or Fisher's exact test, as appropriate. Correlations between serum AIMP1 with SLEDAI-2K and laboratory variables related to either disease activity or inflammatory burden were evaluated by using the Pearson's correlation analysis. The odds ratio (OR) was assessed using multivariate forward logistic regression for all variables with *p*-values <0.20 in univariate analysis. The optimal cut-off value of serum AIMP1 to predict active SLE was evaluated by calculating the area under the receiver operator characteristic curve (AUROC). All statistical analyses were conducted using both GraphPad Prism version 5.0 (GraphPad Software, San Diego, California, USA) and the SPSS package for Windows v. 21 (SPSS Inc., Chicago, Illinois, USA), and two-tailed *p*-values <0.05 were considered statistically significant.

Results

Characteristics of patients with active and stable SLE

The characteristics of SLE patients are shown in Table I. The median age was 41.0 and 90.0% of the patients were female. The median disease duration was 79.0 months. The median SLEDAI-2K and serum AIMP1 were 4.5 and 6.9 ng/ml, respectively. Glucocorticoid was the most commonly administered medication (76.9%), followed by hydroxychloroquine (42.5%) and mycophenolate mofetil (22.5%).

All SLE patients were evenly reclassified as active and stable SLE groups according to the cut-off of SLEDAI of 5 (80 patients for each group). There were no significant differences in age and gender between the two groups, though patients with stable SLE had longer disease durations than those with active SLE. Patients with active SLE had a higher median SLEDAI-2K than those with stable SLE (7.0 *vs*. 2.0, $p<0.001$). In addition, patients with active SLE showed laboratory results closely correlated with increased disease activity of SLE, except for WBC counts and those reflecting extended inflammatory burdens. Patients with active SLE had a higher median serum AIMP1 than those with stable SLE (8.0 *vs*. 6.5 ng/ml, $p<0.001$, Fig. 1). Differences in medications concurrently administered were not statistically apparent between patients with active and stable SLE (Table I).

Comparison of serum AIMP1 between patients with SLE and healthy controls

When we compared serum AIMP1 between patients with SLE and healthy controls, we found that both patients with active and stable SLE showed higher median serum AIMP1 than healthy controls (the median serum AIMP1 of active SLE *vs*. healthy controls and the serum AIMP1 of stable SLE *vs*. healthy controls, all $p<0.001$) (Fig. 1). To evaluate whether a different SLEDAI-2K cut-off value to define active SLE might influence the results of

Table I. Characteristics of SLE patients and comparison between active and stable SLE.

	Total (n=160)	Active SLE (n=80)	Stable SLE (n=80)	*p*-value
Demographic data				
Age (years)	41.0 (30.0-49.5)	40.0 (27.5-47.5)	42.5 (32.0-51.0)	0.071
Female gender (n, (%))	144 (90.0)	74 (92.5)	70 (87.5)	0.293
Disease duration (months)	79.0 (30.6-176.7)	63.2 (3.4-121.5)	101.2 (50.7-212.9)	0.003
SLEDAI-2K	4.5 (2.0-7.0)	7.0 (5.5-9.0)	2.0 (0.0-4.0)	<0.001
Laboratory variables related to disease activity and inflammatory burdens				
Anti-ds DNA (IU/mL)	17.0 (0.0-83.5)	58.0 (15.0-222.0)	0.0 (0.0-21.0)	<0.001
Complement 3 (mg/dL)	73.2 (54.5-97.5)	64.8 (40.7-72.9)	90.9 (73.2-111.8)	<0.001
Complement 4 (mg/dL)	14.0 (8.0-21.1)	9.5 (5.4-14.7)	18.3 (13.2-25.3)	<0.001
White blood cell count (/μL)	5290.0 (3720.0-7035.0)	4995.0 (3015.0-6735.0)	5625.0 (4050.0-7255.0)	0.491
Lymphocyte count (/μL)	1210.0 (760.0-1770.0)	885.0 (540.-1245.0)	1615.0 (1175.0-2125.0)	<0.001
Haemoglobin (g/dL)	12.1 (10.8-13.1)	11.3 (9.4-12.5)	12.9 (11.9-13.6)	<0.001
Platelet count (×1,000/μL)	205.0 (156.0-260.5)	180.0 (106.5-227.5)	234.0 (191.0-279.0)	<0.001
ESR (mm/hr)	28.5 (17.0-47.0)	37.0 (22.0-65.5)	24.0 (15.0-34.5)	<0.001
CRP (mg/L)	1.2 (0.5-3.4)	1.7 (0.9-8.1)	0.7 (0.4-2.3)	0.002
Serum AIMP1 (ng/mL)	6.9 (4.8-9.6)	8.0 (5.1-12.8)	6.5 (4.7-8.4)	<0.001
Medications (n, (%))				
Glucocorticoid	123 (76.9)	63 (78.8)	60 (75.0)	0.575
Hydroxychloroquine	68 (42.5)	29 (36.3)	39 (48.8)	0.111
Cyclophosphamide	3 (1.9)	3 (3.8)	0 (0.0)	0.245
Mycophenolate mofetil	36 (22.5)	15 (18.8)	21 (26.3)	0.258
Tacrolimus	9 (5.6)	5 (6.3)	4 (5.0)	0.999
Azathioprine	14 (8.8)	8 (10.0)	6 (7.5)	0.577

Values are expressed as the median (interquartile range) or n (%).
SLE: Systemic lupus erythematosus; SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; AIMP1: aminoacyl-tRNA synthetase-interacting multifunctional protein-1.

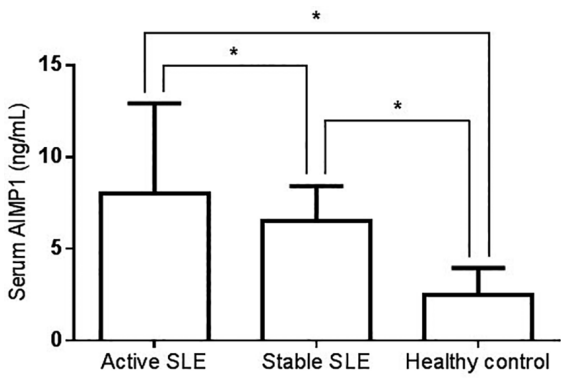

Fig. 1. Comparison of serum AIMP1 between patients with SLE and healthy controls. Both patients with active and stable SLE showed the higher median serum AIMP1 than healthy controls. Data are expressed as medians and the error bars indicate interquartile ranges. *p<0.001.
AIMP1: Aminoacyl-tRNA synthetase-interacting multifunctional protein-1; SLE: Systemic lupus erythematosus.

the study, we re-classified patients included in the study by using a SLEDAI-2K cut-off value of ≥4. Accordingly, a total of 102 patients were classified as active SLE and 58 as stable SLE. Comparison of serum AIMP1 in patients with active SLE (SLEDAI-2K ≥4, n=102) and stable SLE (SLEDAI-2K <4, n=58) showed that median serum AIMP1 was significantly higher in patients with active SLE than those with stable SLE (7.7 *vs*. 6.5 ng/ml, p<0.001), even when a different SLEDAI-2K cut-off value was applied (Fig. 2A).

Comparison of serum AIMP1 among patients with stable SLE

To evaluate the role of serum AIMP1 in identifying patients in remission, we divided patients with stable SLE into three groups: patients with remission, patients with SLEDAI-2K=0, patients with 1 ≤ SLEDAI-2K ≤4. Seven patients were defined as having remission, 17 as SLEDAI-2K = 0, and 56 as 1 ≤ SLEDAI-2K ≤4. However, comparison of serum AIMP1 between the groups showed no significant difference (Fig. 2B).

Correlation of serum AIMP1 with laboratory variables related to either disease activity or inflammatory burdens in patients with SLE

We evaluated the correlation of serum AIMP1 with SLEDAI-2K and laboratory variables related to either disease activity or inflammatory burdens in patients with SLE. Serum AIMP1 was significantly correlated with SLEDAI-2K (r=–0.348, p<0.001) and, furthermore, serum AIMP1 was also correlated with laboratory variables related to either disease activity or inflammatory burdens. Among the laboratory variables, serum AIMP1 was the most strongly correlated with C3 (r=–0.340, p<0.001), followed by haemoglobin (r=–0.302, p<0.001) and anti-ds DNA (r=0.278, p<0.001) (Fig. 3).

Serum AIMP1 is a useful predictive value for active SLE

We calculated the optimal cut-off level for serum AIMP1 to predict active SLE by using ROC analysis. We found that 10.09 ng/ml of serum AIMP1 (AUROC 0.634, 95% confidence interval (CI) 0.554–0.708, p=0.003) was the optimal cut-off to predict active SLE. Finally, we performed univariate and multivariate logistic regression analysis to clarify the potential of serum AIMP1 to predict active SLE based on the SLEDAI-2K. In univariate analysis, serum AIMP1 ≥10.09 ng/ml, anti-ds DNA, C3, C4, WBC, lymphocyte, platelet count, hae-

Table II. Univariate and multivariate logistic regression analysis of predictive values for active SLE.

Laboratory variables	Univariate analysis			Multivariate analysis[¶]		
	Odds ratio	95% CI	*p*-value	Odds ratio	95% CI	*p*-value
Serum AIMP1 ≥10.09 (ng/mL)	5.930	2.412-14.579	<0.001	3.919	1.223-12.564	0.022
Anti-ds DNA (IU/mL)	1.013	1.007-1.020	<0.001			
Complement 3 (mg/dL)	0.945	0.928-0.963	<0.001	0.957	0.938-0.977	<0.001
Complement 4 (mg/dL)	0.890	0.850-0.932	<0.001			
White blood cell count (/μL)	1.000	0.999-1.000	0.489			
Lymphocyte count (/μL)	0.998	0.998-0.999	<0.001	0.999	0.998-0.999	<0.001
Haemoglobin (g/dL)	0.577	0.462-0.720	<0.001			
Platelet count (×1,000/μL)	0.991	0.986-0.995	<0.001			
ESR (mm/hr)	1.036	1.019-1.053	<0.001	1.029	1.007-1.052	0.009
CRP (mg/L)	1.067	1.011-1.126	0.019			

[¶]For the multivariate logistic regression analysis, forward logistic regression for all variables with *p*-values <0.20 in univariate analysis was used.
AIMP1: Aminoacyl-tRNA synthetase-interacting multifunctional protein-1; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

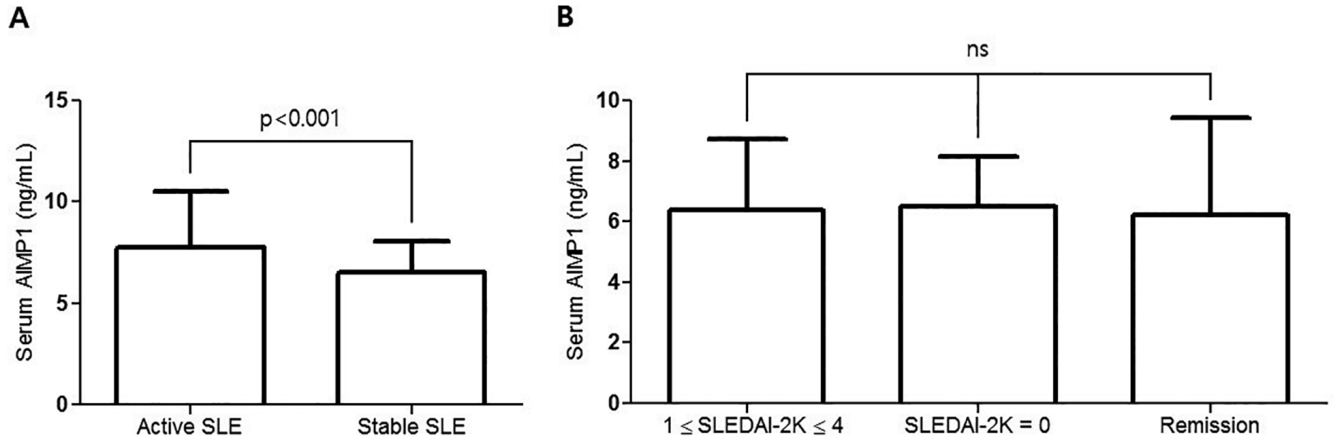

Fig. 2. Serum AIMP1 in patients with active and stable SLE using a different SLEDAI-2K cut-off value and comparison of serum AIMP1 among patients with stable SLE.
Comparison of serum AIMP1 in patients with active and stable SLE using a different definition (SLEDAI-2K ≥4 as active SLE) showed that patients with active SLE had significantly higher serum AIMP1 than those with stable SLE (**A**). Among patients with stable SLE (n=80), difference between serum AIMP1 in patients with remission, SLEDAI-2K = 0, and 1 ≤ SLEDAI-2K ≤ 4 were not noted (**B**). Data are expressed as medians and the error bars indicate interquartile ranges. ns: not significant.
AIMP1: Aminoacyl-tRNA synthetase-interacting multifunctional protein-1; SLE: Systemic lupus erythematosus; SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000.

moglobin, ESR, and CRP were shown to be useful in discriminating active and stable SLE. However, in multivariate analysis, serum AIMP1 ≥10.09 ng/ml (OR 3.919, 95% CI 1.223–12.564, *p*=0.022), C3 (OR 0.957, 95% CI 0.938–0.977, *p*<0.001), lymphocyte count (OR 0.999, 95% CI 0.998–0.999, *p*<0.001), and ESR (OR 1.029, 95% CI 1.007–1.052, *p*=0.009) were revealed to be useful in distinguishing active and stable SLE (Table II).

Discussion

This study, to our best knowledge, is the first to demonstrate a link between the secreted form of AIMP1 in the peripheral blood and disease activity of SLE. To date, several parameters reflecting disease activity of SLE have been proposed (29, 30). Among those parameters, anti-ds DNA and complements have been generally considered to be better laboratory values for assessing disease activity of SLE (31). However, anti-ds DNA, in particular, has a limitation that it cannot accurately predict the rapidly altering disease activity of SLE owing to its relatively long lifespan. Beyond these laboratory parameters, SLEDAI-2K is currently the most widely used index to assess disease activity of SLE and it has an advantage in that it includes both clinical and laboratory features (23). However, SLEDAI-2K also has the disadvantage that it may require a relatively long time and high labour cost to complete. Thus, a need for a single serologic marker to accurately reflect disease activity of SLE and predict active SLE has been raised. With these clinical demands, we believe that the results of this study will provide physicians with valuable information on the role of serum AIMP1 in SLE patients with the following reasons: i) both patients with active and stable SLE had higher serum AIMP1 levels than the healthy controls and, furthermore, level of serum AIMP1 was significantly higher in patients with active SLE than those with stable SLE, similar to anti-ds DNA and complement levels; ii) serum AIMP1 significantly correlat-

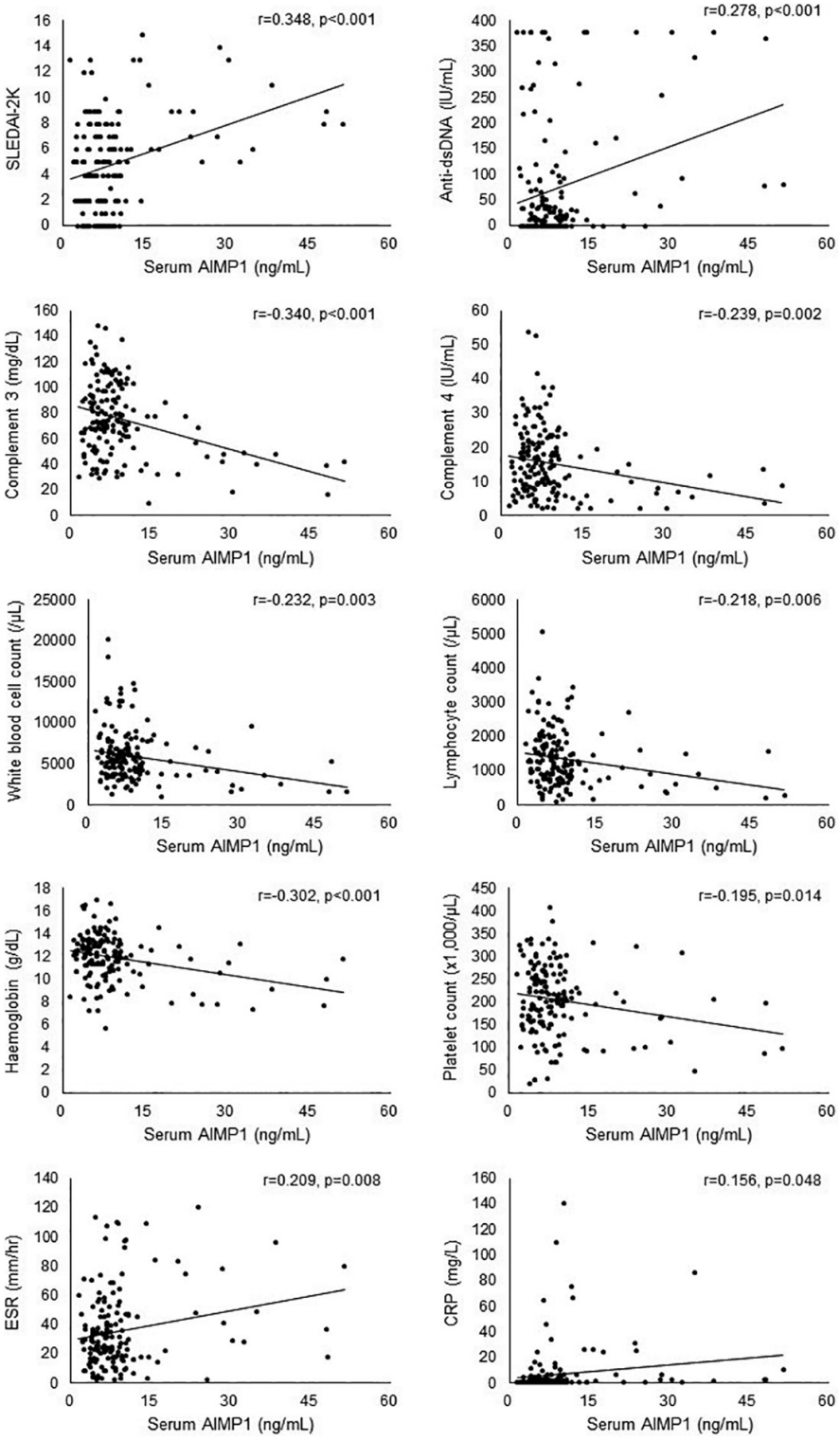

Fig. 3. Correlation of serum AIMP1 with laboratory variables related to either disease activity or inflammatory burdens in patients with SLE.
Serum AIMP1 was significantly correlated with SLEDAI-2K and, furthermore, serum AIMP1 was also correlated with laboratory variables related to either disease activity or inflammatory burden.
SLEDAI-2K: Systemic lupus erythematosus disease activity index-2000; AIMP1: Aminoacyl-tRNA synthetase-interacting multifunctional protein-1; ESR; Erythrocyte sedimentation rate; CRP: C-reactive protein.

ed with not only SLEDAI-2K itself, but also anti-ds DNA and C3; iii) when we set the optimal cut-off of serum AIMP1 level at 10.09 ng/ml, the risk of active SLE in patients having serum AIMP1 higher than the optimal cut-off was significantly higher than that in those having AIMP1 levels below the cut-off; and iv) in multivariate logistic regression, serum AIMP1 level higher than the optimal cut-off level was found to be useful in predicting active SLE.

In the pathogenesis of early SLE, the pioneer autoreactive immune cells are dendritic cells and B cells, which produce interferon–α and autoantibodies, respectively (32, 33). Subsequently, various inflammation-related intracellular signalling molecules may activate p38 MAPK and NF-κB, which can, in turn, accelerate the expression of pro-inflammatory cytokines including interferon-γ, IL-1, IL-2, IL-6, IL-12, IL-17, and TNF-α (9-11). These shifts to a pro-inflammatory status can provoke immunologic alterations such as reduced number and function of Treg cells (34) and enhanced function of follicular T cells (35), which can drive auto-reactive B cells to produce autoantibodies, leading to organ-damage via immune-complex deposition (36). Likewise, when AIMP1 is secreted into the peripheral blood, serum AIMP1 can increase the expression of IL-1, IL-6, IL-8, IL-12 and TNF-α via p38 MAPK and NF-κB (17). Furthermore, AIMP1 might be considered to contribute to the process of inflammation earlier than TNF-α. We found that the pathophysiology of SLE and the immunologic roles of serum AIMP1 shared common intracellular signalling, transcription factors, and pro-inflammatory cytokines. Therefore, through this cross-talk between the two different signals, serum AIMP1 could reflect disease activity of SLE and could be used to predict active SLE, comparable to the traditional activity-reflecting parameters anti-ds DNA and C3.

We also analysed the association between clinical features and serum AIMP1. When we divided patients into two groups according to the optimal cut-off of AIMP1, 36 (22.5%) patients had serum AIMP1 ≥10.09 ng/ml. At the time of blood collection, patients with serum AIMP1 ≥10.09 ng/ml presented with skin rash (19.4% *vs*. 4.8%, p=0.005), oral ulcer (11.1% *vs*. 0.0%, p=0.002), serositis (16.7% *vs*. 4.0%, p=0.009) and lupus nephritis (47.2% *vs*. 25.0%, p=0.011) more frequently than

those having serum AIMP1 <10.09 ng/ml. However, there were no statistically significant differences in photosensitivity, arthritis, and neurological abnormality between the two groups. Although the cause for a relationship between serum AIMP1 and a specific organ involvement observed in this study remains unclear, these results further suggest the probable association between serum AIMP1 and clinical features of SLE.

The strength of our study is that we included a relatively large number of patients with SLE and this is the first study to evaluate the clinical significance of serum AIMP1 in patients with SLE. However, our study has several limitations. First, the clinical and laboratory data were collected retrospectively by reviewing the medical records. In addition, serum AIMP1 measurement was performed only in SLE patients with available stored serum samples. This might have resulted in patient selection bias. Second, this study did not conduct a mechanistic investigation regarding the role of AIMP1 in SLE. Third, as this was a cross-sectional study, serum AIMP1 was not serially measured in patients with active SLE following disease control. Data regarding the changes of AIMP1 following treatment is required to further evaluate the clinical significance of serum AIMP1 in assessing SLE disease activity. Fourth, serum AIMP1 itself was not predictive of disease remission as serum AIMP1 level was not different between patients with remission and without remission among those with stable SLE. Fifth, the correlation between serum AIMP1 and novel biomarkers in SLE (including anti-C1q antibodies) could not be evaluated, as it were not clinically available in our institute. Future studies with a large number of patients which include *in vitro* and *in vivo* experiments will enlighten the role of secretory form of AIMP1 in assessing disease activity and in the pathogenesis of SLE.

In conclusion, serum AIMP1 was associated with disease activity of SLE and could predict active SLE based on the SLE disease activity index SLEDAI-2K. Additional studies are required to elucidate the role of secreted serum AIMP1 in the pathogenesis of SLE.

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