Serum soluble interleukin-7 receptor alpha levels are negatively correlated with the simultaneous activity of antineutrophil cytoplasmic antibody-associated vasculitis

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Abstract

Objective

This study investigated whether serum soluble interleukin-7 receptor alpha (sIL-7Rα) levels could reflect the simultaneous activity of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods

Sixty patients with AAV were included in this study. AAV-related variables and clinical and laboratory data were collected at the two-time points (at early high and late low BVAS) for each patient along with blood sampling. Serum sIL-7Rα levels and the populations of CD3+CD4+ and CD3+CD8+ T cells expressing membranous IL-7Rα (mIL-7Rα) were compared between patients at different time points and between patients and healthy controls.

Results

Serum sIL-7Rα levels were significantly lower in AAV patients at early high BVAS than in those at late low BVAS, and the direction of change in serum sIL-7Rα levels increased as BVAS decreased. Serum sIL-7Rα levels were inversely correlated with BVAS, erythrocyte sedimentation rate and C-reactive protein levels. In addition, serum sIL-7Rα levels in AAV patients at early high BVAS exhibited significantly lower levels than those in healthy controls. Particularly, AAV patients at early high BVAS showed significantly increased populations of CD3+ T cells and CD3+CD8+ T cells expressing mIL-7Rα compared to those at late low BVAS.

Conclusion

This study demonstrated that not only serum sIL-7Rα levels but also the populations of CD3+ and CD3+CD8+ T cells expressing m IL-7Rα were negatively correlated with simultaneous BVAS in patients with AAV. Therefore, we suggest that serum sIL-7Rα levels can be an additional and useful biomarker for assessing the simultaneous activity of AAV.

Key words

soluble receptor, IL-7, antineutrophil cytoplasmic antibody, vasculitis, activity

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Introduction

Interleukin (IL)-7, primarily produced by stromal cells in the bone marrow and thymus, plays an important role in the proliferation of T cells and is known to contribute to immunity in humans (1, 2). The receptor for IL-7 comprises of two components: IL-7 receptor alpha-chain (IL-7Rα, CD127) and common cytokine receptor gamma-chain (γ_c, CD132) (3). Once IL-7 binds to its receptor and crosslinks the extracellular domains of IL-7Rα and γc, Janus kinase (JAK)-1 linked to IL-7Rα and JAK-3 linked to γc may meet and phosphorylate each other, leading to augmentation of intracellular signals of the two kinases via the signal transducer and activator of transcription (STAT) (4). In terms of autoimmunity, it has been demonstrated that IL-7 and IL-7Rα participate in the pathogenesis of several autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, and systemic lupus erythematosus (5-7). Recently, a soluble form of IL-7Rα (sIL-7Rα) has been introduced; however, its role in the pathogenesis of several diseases remains controversial. sIL-7Rα may reduce IL-7 activity, whereas it may conversely promote IL-7 bioactivity (8, 9). In particular, it has been reported that sIL-7Ra could be used as a biomarker that reflects the degree of inflammation because synovial cells produce sIL-7Ra in response to proinflammatory cytokines in rheumatoid arthritis (10).

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic vasculitis that invades small vessels and can thus develop a variety of systemic symptoms (11). AAV comprises of the following three subtypes, according to the clinical features: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic GPA (EGPA) (12). The proinflammatory cytokines and autoreactive immune cells involved in the pathogenesis of autoimmune diseases are also major participants in the immunopathologic mechanism of AAV (13). Therefore, it can be assumed reasonably that serum sIL-7Ra levels may be a useful biomarker in assessing the simultaneous activity of AAV, although it is unclear whether the association between serum sIL-7Ra levels and the inflammatory burden is proportional or inverse. No studies have investigated the clinical significance of serum sIL-7Rα levels in patients with AAV. Hence, this study investigated whether serum sIL-7Rα levels could reflect the simultaneous activity of AAV.

Materials and methods

Patients

Sixty patients with AAV were randomly selected from the Severance Hospital ANCA-associated Vasculitides (SHAVE) cohort, and were included in this study. The SHAVE cohort is a prospective and observational cohort of patients with MPA, GPA, and EGPA, and was initiated in November 2016. Only patients with AAV who satisfied the inclusion criteria were enrolled in the SHAVE cohort, as described in our previous studies (14, 15). The inclusion and exclusion criteria were as follows: i) the classification of AAV should be first made by specialised rheumatologists at Yonsei University College of Medicine and Severance Hospital; ii) AAV diagnosis should be completed only when the 2007 European Medicines Agency algorithms for AAV and polyarteritis nodosa and the 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides criteria were simultaneously fulfilled (11, 12); iii) at diagnosis, patients with AAV, who had concomitant malignancies, serious infectious diseases requiring hospitalisation, and systemic vasculitis other than AAV, were excluded from the cohort; iv) prior to the diagnosis, patients with AAV, who had received immunosuppressive drugs for treating AAV, were excluded from the cohort. Co-existing serious medical conditions and immunosuppressive drug use were identified using the 10th edition of the International Classification Diseases and the Korean Drug Utilization Review system, respectively. This study was approved by the Institutional Review Board (IRB) of Severance Hospital (4-2016-0901) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was

obtained from the patients at the time of enrolment in the SHAVE cohort and blood sampling. The IRB waived the need for written informed consent if it was previously obtained while entering the SHAVE cohort.

Study protocol

At first diagnosis or relapse, the time point showing the highest Birmingham vasculitis activity score (BVAS) before the start of treatment was defined as an early high BVAS, whereas the time point showing the lowest BVAS state after treatment was defined as a late low BVAS.

AAV-related variables and clinical and laboratory data were collected at the two-time points (at early high and late low BVAS) for each patient along with blood sampling.

AAV activity

The AAV subtypes, ANCA type, and AAV-specific indices were reviewed.

In the SHAVE cohort, BVAS is generally obtained for 6 months from the time of enrolment (16). BVAS version 3 was evenly applied to patients with all AAV subtypes to unify the scoring system, despite BVAS for Wegener's granulomatosis (identical to GPA) (17).

Clinical and laboratory data

Age and sex were collected as demographic data. Acute phase reactants, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were also measured (18). Immunoassays were used as the primary screening method for ANCA; however, when patients were found to be negative for ANCA by an antigen-specific assay but positive for perinuclear (P)-ANCA or cytoplasmic (C)-ANCA by an indirect immunofluorescence assay, they were considered to have myeloperoxidase (MPO)-ANCA or proteinase 3 (PR3)-ANCA when AAV was strongly suspected based on the clinical and laboratory features (19).

Measurement of serum sIL-7Rα levels

Whole blood was collected after obtaining patient consent, and sera were isolated and stored at -80°C. All AAV-specific indices were assessed, and tests for acute phase reactants were performed on the day of blood collection. Serum IL-7Ra levels in stored in the sera were measured using enzyme-linked immunosorbent assay kits (Ray Biotech, Inc., Peachtree Corners, GA, USA), according to the manufacturer's instructions. Serum sIL-7Rα measurements were performed twice consecutively (at early high and late low BVAS) in the same patient.

Table I. Characteristics of 60 patients with early high BVAS and late low BVAS AAV (Paired analyses).

Variables	AAV patients at early high BVAS	AAV patients at late low BVAS	*p*-value
At collecting data and blood samples			
Demographic data			
Age (years)	63.0 (21.0)	64.0 (21.0)	<0.001
Female sex (n, (%))	21 (35.0)		N/A
Newly diagnosed disease	45 (75.0)		
Relapsing disease	15 (25.0)		
Disease duration (month)	0.0 (5.0)	13.5 (11.0)	N/A
AAV subtypes (n, (%))			
MPA	29 (48.3)		N/A
GPA	19 (31.7)		N/A
EGPA	12 (20.0)		N/A
ANCA positivity (n, (%))			
MPO-ANCA (or P-ANCA) positivity	40 (66.7)	24 (40.0)	0.008
PR3-ANCA (or C-ANCA) positivity	7 (11.7)	7 (11.7)	0.973
Both ANCAs	1 (1.7)	0 (0)	1.000
BVAS	11.5 (12.0)	4.0 (2.0)	<0.001
Clinical features (n, (%))			
General manifestations	27 (45.0)	2 (3.3)	<0.001
Cutaneous manifestations	10 (16.7)	6 (10.0)	0.283
Mucous and ocular manifestations	2 (3.3)	3 (5.0)	1.000
Otorhinolaryngologic manifestations	25 (41.7)	22 (36.7)	0.575
Pulmonary manifestations	44 (73.3)	33 (55.0)	0.036
Cardiovascular manifestations	5 (8.3)	1 (1.7)	0.207
Gastrointestinal manifestations	2 (3.3)	0 (0.0)	0.496
Renal manifestations	34 (56.7)	29 (48.3)	0.361
Nervous system manifestations	20 (33.3)	18 (28.6)	0.695
Acute phase reactants			
ESR (mm/hr)	33.0 (74.0)	15.0 (18.0)	<0.001
CRP (mg/L)	5.2 (36.6)	1.5 (3.8)	0.003
Serum sIL-7Rα levels (ng/mL)	15.2 (9.5)	18.2 (30.0)	0.005
From diagnosis to the time at collecting data and blood samples			
Medications administered (n, (%))			
Glucocorticoids	14 (23.3)	59 (98.3)	
Cyclophosphamide	10 (16.7)	40 (66.7)	
Rituximab	2 (3.3)	16 (26.7)	
Azathioprine	6 (10.0)	47 (78.3)	
Mycophenolate mofetil	1 (1.7)	18 (30.0)	
Tacrolimus	0 (0.0)	9 (15.0)	
Methotrexate	2 (3.3)	10 (16.7)	

Values are expressed as a median (interquartile range, IQR) or N (%).
ANCA: antineutrophil cytoplasmic antibody; AAV: ANCA-associated vasculitis; BVAS: Birmingham vasculitis activity score; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; C: cytoplasmic; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; sIL-7Rα: soluble interleukin-7 receptor-α; N/A: not applicable.

Healthy controls

The serum samples obtained from 60 healthy controls were provided by the Healthcare Centre of Severance Hospital. Serum sIL-7Rα levels were measured in the provided sera and compared with those of AAV patients at early high BVAS. The use of clinical data from healthy controls was approved by the IRB of Severance Hospital (4-2017-0761).

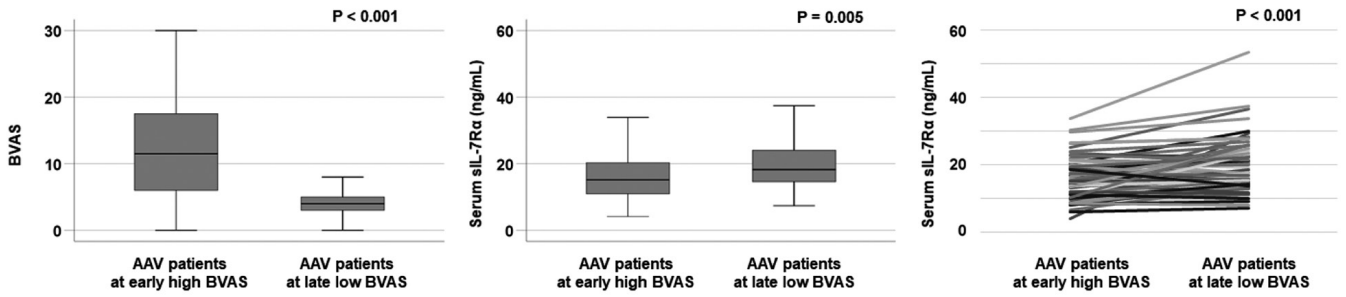

Fig. 1. Comparison of serum sIL-7Rα levels between AAV patients at early high and those at late low BVAS.
Serum sIL-7Rα levels are significantly lower in AAV patients at early high BVAS than in those at late low BVAS and the direction of change in serum sIL-7Rα levels increases as BVAS decreases.
sIL-7Rα: soluble interleukin-7 receptor alpha; BVAS: Birmingham vasculitis activity score; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody.

Table II. Correlation analysis of serum sIL-7Rα levels with BVAS, the sum of the scores assigned to each systemic item of BVAS and acute phase reactants.

Variables	Correlation coefficient (r)	*p*-value
Both AAV patients at early high BVAS and those at late low BVAS		
BVAS	-0.189	0.039
Clinical features		
General manifestations	-0.318	<0.001
Cutaneous manifestations	-0.173	0.058
Mucous and ocular manifestations	0.007	0.943
Otorhinolaryngologic manifestations	-0.163	0.076
Pulmonary manifestations	-0.109	0.237
Cardiovascular manifestations	0.003	0.977
Gastrointestinal manifestations	-0.102	0.266
Renal manifestations	0.013	0.886
Nervous system manifestations	-0.189	0.038
Acute phase reactants		
ESR (mm/hr)	-0.305	0.001
CRP (mg/L)	-0.317	0.001

sIL-7Rα: soluble interleukin-7 receptor-α; BVAS: Birmingham Vasculitis Activity Score; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

Table III. Comparison of serum sIL-7Rα levels in each AAV subtypes.

AAV subtypes	Patients at early high BVAS (ng/mL)	*p*-value	Patients at late low BVAS (ng/mL)	*p*-value
MPA	14.7 (11.3)		19.4 (9.8)	
GPA	15.2 (9.1)	0.584	17.5 (8.1)	0.889
EGPA	16.4 (10.5)		19.7 (12.6)	

Values are expressed as a median (interquartile range, IQR) or N (%).
AAV: ANCA-associated vasculitis; BVAS: Birmingham vasculitis activity score; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; sIL-7Rα: soluble interleukin-7 receptor-α.

IL-7R expression of CD3+ T cells

Stored peripheral blood mononuclear cells (PBMCs) were collected from nine patients with AAV among the 60 patients in this study. Similar to the measurement of serum sIL-7Rα levels, analyses using fluorescence-activated cell sorting of PBMCs were performed twice: at early high and late low BVAS. PMBCs were thawed and cross-sectional sections were stained with the following antibodies: anti-CD3-V500 and anti-CD8-V450 (BD Biosciences, Oxford, UK) and anti-CD4-Alexa Fluor 700, and anti-CD-127-PE (BioLegend, CA, USA). The cells were analysed using the FACSVerse and FlowJo software (BD Biosciences, Oxford, UK).

Statistical analyses

All statistical analyses were performed using IBM SPSS Statistics for Windows, v. 26. (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as medians with interquartile ranges, whereas categorical variables are expressed as numbers (percentages). Significant differences between two continuous variables were compared using the Mann-Whitney U-test. Significant differences between two paired samples were analysed using the Wilcoxon signed-rank test. The correlation coefficient (r) between two variables was determined using the Pearson's correlation analysis. Statistical significance was set at $p<0.05$.

Results

Comparison of the characteristics of patients with AAV between early high BVAS and late low BVAS

Twenty-nine patients were classified as MPA, 19 were as GPA, and 12 were as EGPA.

At the time of enrolment, 45 (75.0%) patients were newly diagnosed and 15 (25.0%) patients were relapsed. The median time interval between the early high BVAS and late low BVAS states was 13.5 months. As for ANCA positivity, the frequency of MPO-ANCA (or P-ANCA) positivity in AAV patients at early high BVAS was significantly higher than that in AAV patients at late low BVAS. Among 9 systemic manifestations of AAV, there were significant differences in general and pulmonary manifestations between AAV patients at early high BVAS and those at late low BVAS (Table I). The median val-

ues of BVAS and serum sIL-7Rα levels are presented in Figure 1. The median BVAS in AAV patients at early high BVAS was much higher than in those at late low BVAS (11.5 *vs*. 4.0, $p<0.001$), as the name of each group suggests. Contrary to the direction of change in BVAS, serum sIL-7Rα levels were significantly lower in AAV patients at early high BVAS than in those at late low BVAS (15.2 *vs*. 18.2, $p=0.005$). In addition, comparison analysis by Wilcoxon signed-rank test demonstrated that the direction of change in serum sIL-7Rα levels increased as BVAS decreased ($p<0.001$) (Fig. 1).

Correlation analysis of serum sIL-7Rα levels with BVAS, the sum of the scores assigned to each systemic item of BVAS and acute phase reactants

Correlation analysis of serum sIL-7Rα levels with variables was performed in patients with AAV at early high and late low BVAS. Serum sIL-7Rα levels were significantly and inversely correlated with simultaneous BVAS (r=-0.189). In AAV patients at early high BVAS and those at late low BVAS, serum sIL-7Rα levels were negatively correlated with the sum of the scores assigned to general (r=-0.318) and nervous system manifestations (r=-0.189). In addition, serum sIL-7Rα levels were significantly correlated with ESR (r=-0.305) and CRP (r=-0.317) (Table II).

Comparison of serum sIL-7Rα levels between patients with early high BVAS and late low BVAS in AAV subtypes

Since MPA, GPA, EGPA are different diseases, we analysed whether there was a difference in the serum sIL-7Rα levels according to each subtype, and as a result, there was no difference (Table III). Furthermore, longitudinal changes in serum sIL-7Rα levels according to each subtype were analysed. As a result, serum sIL-7Rα levels were significantly increased after treatment in MPA and GPA patients. In addition, serum sIL-7Rα levels in EGPA patients tended to increase after treatment, although it was not statistically significant (Supplementary Fig. S1).

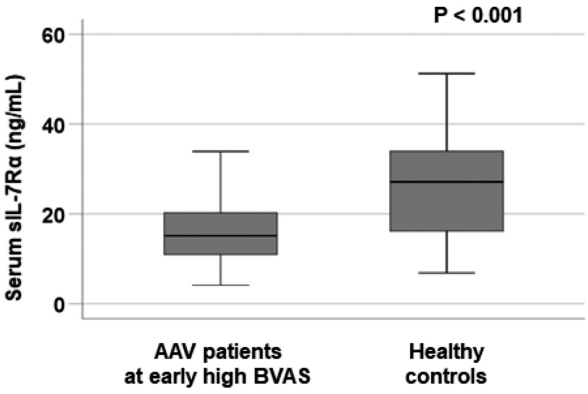

Fig. 2. Comparison of serum sIL-7Rα levels between AAV patients at early high BVAS and healthy controls.
Serum sIL-7Rα levels are significantly lower in AAV patients at early high BVAS than those in healthy controls.
sIL-7Rα: soluble interleukin-7 receptor alpha; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; BVAS: Birmingham vasculitis activity score.

Comparison of serum sIL-7Rα levels between AAV patients at early high BVAS and healthy controls

AAV patients at early high BVAS exhibited a significantly lower level of serum sIL-7Rα than healthy controls (15.2 ng/mL *vs*. 27.1 ng/mL, $p<0.001$) (Fig. 2).

Comparison of the population of CD3+ T cells expressing CD127 between early high and late low BVAS

CD127+ indicates the cell membrane-bound form of IL-7Rα (m IL-7Rα). AAV patients at early high BVAS showed a significantly lower population of CD3+CD127+ T cells than those at late low BVAS (62.6% *vs*. 78.6%, $p=0.015$). In addition, patients at early high BVAS exhibited a significantly lower population of CD3+CD8+CD127+ T cells than those at late low BVAS (29.5% *vs*. 63.9%, $p=0.024$). However, the population of CD3+CD4+CD127+ T cells did not differ between patients at early high or late low BVAS (Fig. 3).

Discussion

This study investigated whether serum sIL-7Rα levels could reflect the simultaneous activity of AAV. The findings were as follows: first, serum sIL-7Rα levels were significantly lower in AAV patients at early high BVAS than in those at late low BVAS, and the direction of change in serum sIL-7Rα levels increased as BVAS decreased ($p<0.001$). Second, serum sIL-7Rα levels were inversely correlated with BVAS, ESR and CRP levels. Moreover, it was negatively correlated with the sum of the scores assigned to general and nervous system manifestations. Third, serum sIL-7Rα levels in AAV patients at early high BVAS exhibited significantly lower levels than those in healthy controls. Fourth, T cells expressing mIL-7Rα tended to decrease as BVAS increased. In particular, AAV patients at early high BVAS showed significantly decreased populations of CD3+ T cells and CD3+CD8+ T cells expressing mIL-7Rα compared to those at late low BVAS. Therefore, it was concluded that the increased concentration of serum IL-7 may provoke major organ damages as a proinflammatory cytokine, leading to an increase in BVAS, and may paradoxically act as a suppressor and diminish the expression of mIL-7Rα and sIL-7Rα genes in AAV patients with high BVAS.

The IL-7 receptor is a dimeric protein comprising of IL-7Rα linked to JAK-1 and γ_c bound to JAK-3. When IL-7 binds to membrane-bound receptors for IL-7, particularly, mIL-7Rα, JAK-1 phosphorylates STAT5. Subsequently, phosphorylated STAT5 translocates into the nucleus, binds to the promoter, and acts as a transcription factor (20). mIL-7Rα is usually expressed on the surface of stromal cells in the thymus and lymphoid tissues (4). Therefore, through mIL-7Rα, IL-7 is involved in T lymphopoiesis in the thymus and is associated with the homeostasis and proliferation of T cells as well as the survival of effector and memory T cells. Conversely, IL-7 negatively regulates inhibitory signals such as programmed cell death protein 1 and transforming growth factor-beta (21). On the other hand, sIL-7Rα is a truncated form of mIL-7Rα that is expressed by

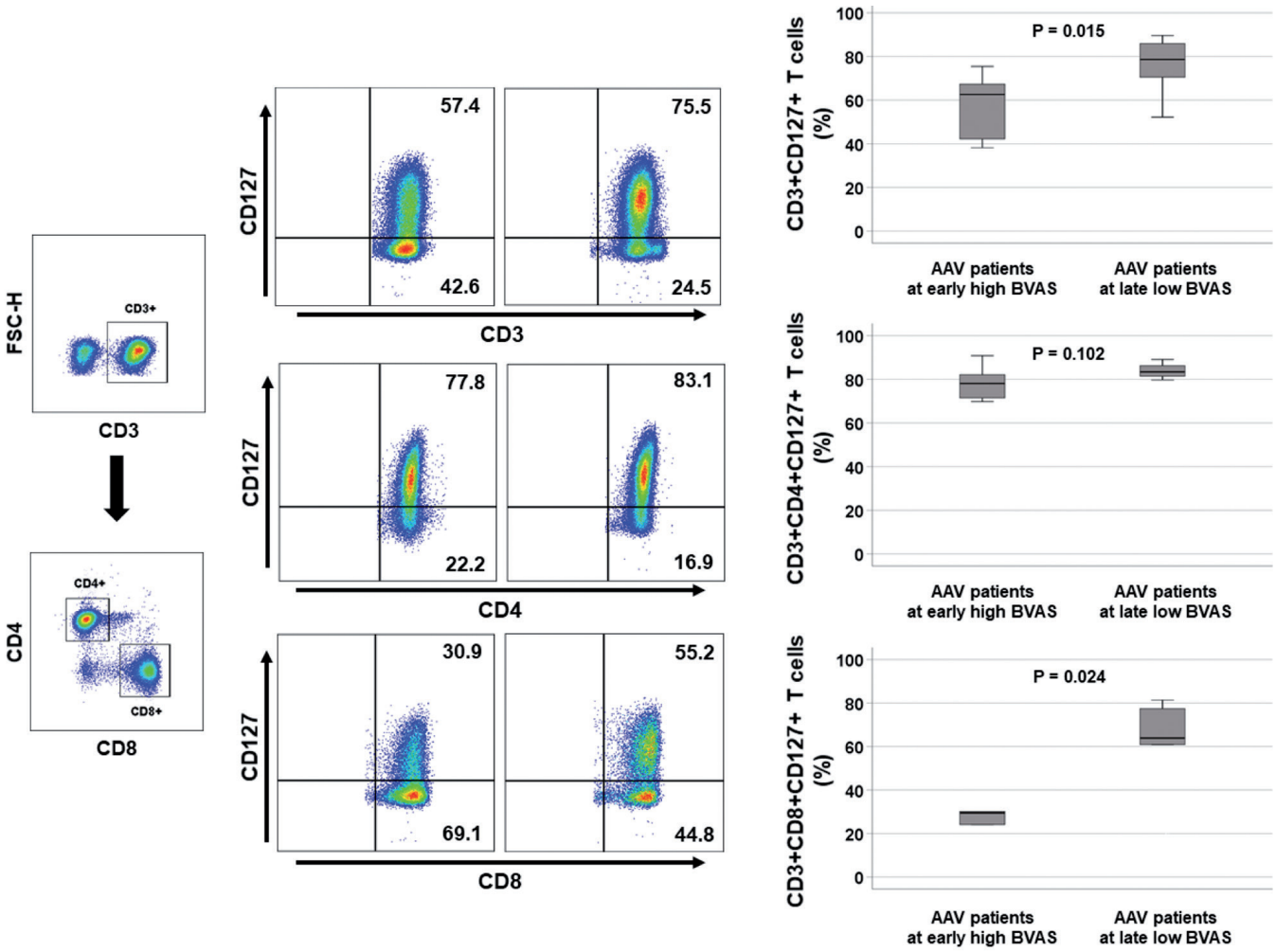

Fig. 3. Comparison of the population of T cells expressing CD127 between AAV patients at early high BVAS and those at late low BVAS.
AAV patients at early high BVAS show a significantly higher population of CD3+CD127+ T cells as well as CD3+CD8+CD127+ T cells than those at late low BVAS.
sIL-7Rα: soluble interleukin-7 receptor alpha; AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; BVAS: Birmingham vasculitis activity score.

alternative splicing of the same encoding genes. Unlike mIL-7Rα, sIL-7Rα has paradoxical dual effects on IL-7: a direct antagonistic effect on IL-7 as a scavenger and an indirect agonistic effect on IL-7 by promoting IL-7 bioactivity (9, 22). Given that a high concentration of IL-7 has been reported to reduce the expression of mIL7-Ra, IL-7 may act as a negative regulator of IL-7Rα expression (4, 22).

Herein, in AAV patients with high BVAS, in whom the concentration of IL-7 may be considered high, serum sIL-7Ra was significantly decreased, and the population of CD8+ T cells expressing mIL-7Ra was also significantly lower. Conversely, in patients with low BVAS, in whom serum IL-7 levels may be expected to be low, serum sIL-7Ra was significantly increased, and the population of CD8+ T cells expressing mIL-7Ra was also significantly higher. CD4+ T cells showed a similar pattern to CD8+ T cells; however, the difference was not statistically significant. Meanwhile, sIL-7Ra has been reported to amplify IL-7 induced CD8+ T cell proliferation. Therefore, it is reasonable to assume that an increase in the population of CD8+ T cells expressing mIL-7Ra may be affected by enhanced serum sIL-7Ra levels (22). We conclude that serum sIL-7Ra showed an inverse association with the activity of BVAS; therefore, it is believed that this study discovered the clinical potential of serum sIL-7Ra as an additional biomarker to predict the cross-sectional activity of AAV.

There were discrepancies between AAV and other autoimmune diseases in the pattern of serum sIL-7Rα levels to reflect the simultaneous activity of diseases. A previous study reported that serum sIL-7Rα levels were strongly associated with lupus nephritis and were increased in patients with lupus nephritis compared with healthy controls (23). Previous studies demonstrated that IL-7Rα expression in synovial tissues of patients with rheumatoid arthritis was significantly elevated compared to patients with non-inflammatory arthritis (24) and that synovial fibroblasts could produce sIL-7Rα in response to inflammatory cytokines (10). In addition, serum sIL-7Rα produced and secreted from T cells in patients with infectious diseases was augmented and

its level was significantly higher than that in healthy controls (25). Based on the above results, it can be speculated that the expression and production of sIL-7Rα may be proportional to the extent of inflammation. Meanwhile, the results of this study were in disagreement with this concept. As the immunopathologic mechanisms of IL-7, mIL-7Rα, and sIL-7Rα have not been clearly elucidated, it is impossible to explain this discrepancy between AAV and other autoimmune diseases. Nevertheless, given that the immunological role of CD3+CD8+ T cells is considered relatively more important in AAV (26, 27), we suggest the possibility of the presence of a triangular association between IL-7, sIL-7Rα, and the population of CD3+CD8+ T cells in the pathophysiology of AAV.

Strengths

The merit of this study is that for the first time, we demonstrated that serum sIL-7Rα levels could reflect the simultaneous activity of AAV and suggest its clinical use as a biomarker for assessing the pattern of changes in BVAS.

Limitations

This study has several limitations. Most importantly, the number of patients was not large enough to represent patients with AAV in real clinical settings owing to a single-centre study. The results of this study were obtained by collecting and analysing clinical and laboratory data including BVAS and serum sIL-7Rα at only two different time points. The results obtained by analysing the data collected at more time points would have been more reliable. We did not have diseased control group other than AAV. The results analysing and comparing the data with other diseased control group would have provided more information. Since the correlation coefficient between serum sIL-7Rα levels and BVAS is low, immediate clinical application is limited. However, given that BVAS has a limitation in reflecting the current disease activity sensitively because it is composed of nine heterogeneous systemic items, and includes both acute and chronic clinical manifestations (28), this study has the clinical implications as a pilot study suggesting an additional and novel serologic biomarker for the activity of AAV. The results that serum sIL-7Rα levels were significantly correlated with ESR and CRP may also support our assertion. Finally, although this study asserted a hypothesis of the immunopathologic mechanism of serum sIL-7Rα being inversely correlated with BVAS based on the results, it could not prove a direct and clear mechanism. However, we believe that this study will be a cornerstone for future studies, as it is the first pilot study to investigate the clinical implications of serum sIL-7Rα levels in patients with AAV.

Conclusion

In conclusion, for the first time, this study demonstrated that serum sIL-7Rα levels were inversely correlated with BVAS and revealed that the populations of CD3+ T cells and CD3+CD8+ T cells expressing m IL-7Rα were also negatively proportional to the activity in patients with AAV. Our results offer new insights into the potential immunological role of sIL-7Rα in AAV and provide novel biomarkers of disease activity in AAV. Therefore, we suggest that serum sIL-7Rα levels can be an additional and useful biomarker for assessing the simultaneous activity or predicting future negative changes in activity in patients with AAV.

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