

ORIGINAL ARTICLE

Differences Between Juvenile-onset Ankylosing Spondylitis and Adult-onset Ankylosing Spondylitis

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, which involves the spine, peripheral joints and entheses. Juvenile-onset ankylosing spondylitis (JAS) affects children under the age of 16 years. JAS has been noted to present as clinical courses different from those of adult-onset ankylosing spondylitis (AAS). Therefore, the purpose of the present study was to compare the possible risk factors, clinical manifestations, laboratory markers, radiological changes, and functional outcome between these 2 patient groups.

Methods: AS patients were enrolled from the rheumatologic clinic of a tertiary medical center from January 1 to June 30 in 2006. The demographic data, clinical symptoms/signs, Bath AS indices, HLA-B27, inflammatory markers, radiological findings, and treatment history were acquired with questionnaires, clinical evaluation, and chart review. The differences between JAS and AAS patients were evaluated and analyzed.

Results: A total of 169 patients (142 males, 27 females) were included, comprising 47 JAS and 122 AAS patients. The ages of onset were 12.8 ± 2.7 years and 25.0 ± 7.4 years for JAS and AAS, respectively. They had similar gender distribution, years of delay to diagnosis and disease duration. A substantial proportion of our patients (40.4% of JAS and 34.4% of AAS) had physical trauma in the 1 month before disease onset. Also, 22.7% of JAS patients had intense physical training, while 25.2% of AAS patients did heavy work during the period. The first manifestation of JAS was mainly peripheral enthesopathy or arthritis, but axial symptoms in most AAS. More JAS patients had peripheral enthesopathies and arthritis on any occasion. Although there was a trend of higher score in Bath AS Disease Activity Index (BASDAI), Bath AS Metrology Index (BASMI) and Physician's Global Assessment (PGA) score, JAS patients had a comparable Bath AS Functional Index (BASFI) and Bath AS Patient's Global Assessment (BAS-G) as AAS patients. As to the laboratory and radiological tests, JAS patients had higher levels of C-reactive protein and erythrocyte sedimentation rate, and more radiographic changes of hip joints.

Conclusion: JAS and AAS patients had distinct presentations. JAS presented more peripheral enthesopathies and arthritis at disease onset and at any time of the course. If treated effectively, JAS will not lead to a worse functional outcome than AAS. Therefore, it is mandatory to diagnose and treat JAS as early as possible. [*J Chin Med Assoc* 2009;72(11):573–580]

Key Words: adult-onset ankylosing spondylitis, Bath ankylosing spondylitis indices, juvenile-onset ankylosing spondylitis, modified Stoke Ankylosing Spondylitis Spinal Score

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease, which involves the spine, peripheral joints and entheses. By definition, juvenile-onset ankylosing

spondylitis (JAS) is when the onset of AS occurs at less than 16 years of age.¹ In previous studies, the prevalence of JAS in AS patients varied from 9% to 21% in Caucasian populations, but was $\geq 40\%$ in Mexican Mestizo and Korean AS patients.² In daily practice, we



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have noted that patients with JAS and adult-onset ankylosing spondylitis (AAS) have different clinical manifestations. Some studies found that delayed diagnosis, joint deformity, and functional impairment were more frequent in patients with JAS than AAS.^{3,4} Another study observed a comparable functional outcome between JAS and AAS patients.⁵ A recent study reported that AAS was associated with worse functional and quality of life measures, and higher fatigue scores, after adjustment for disease duration.⁶

Do JAS and AAS patients have different disease courses because of different etiologies? HLA-B27 was noted to be closely related to AS in 1973. Some other genes, such as HLA-B60, B61, CYP2D6, and interleukin-1 β , were later found to relate to AS.⁷ In previous studies, gastrointestinal (GI)/genitourinary (GU) infection was shown to be associated with spondyloarthropathies (SpAs). The pathogens *Klebsiella pneumoniae*, *Salmonella enteritidis*, and *Escherichia coli* were found to relate to AS.⁸⁻¹³ Physical trauma was also believed to trigger the development of SpAs in several reports.¹⁴⁻¹⁷ New antigens released from trauma,¹⁸ deep Koebner's phenomenon,¹⁹ and neuropeptide substance P released from peripheral nerve terminals²⁰ were suggested to initiate the autoimmune reactions of SpAs in physical trauma. However, some authors have not identified this phenomenon.^{21,22} In this study, we compared the possible risk factors of AS, such as HLA-B27, GI/GU infection, physical trauma, intense physical training and heavy working in JAS and AAS.

Until now, there have been no integral comparisons of clinical manifestations, disease activity, radiological and functional outcomes between JAS and AAS groups in Chinese populations. The present study was undertaken to compare the disease courses of these 2 patient groups in Taiwan.

Methods

Subjects

We enrolled AS patients who visited the rheumatologic clinic of a tertiary medical center during the period from January 1 to June 30 in 2006. All of the patients fulfilled the 1984 modified New York criteria for AS. Patients were included if they had received regular follow-up at the clinic for more than 3 months, and taken prescribed medication (including nonsteroidal anti-inflammatory drugs [NSAIDs], corticosteroids, disease-modifying antirheumatic drugs [DMARDs], antitumor necrosis factors [anti-TNF], or other symptomatic treatment) with good compliance ($\geq 90\%$) in the 3 months prior to the interviewing day. A total of

169 patients (142 males, 27 females) entered into our series. Each participant provided informed consent, and the performance of this study was approved by the research ethics committee of the hospital.

Questionnaire

During face-to-face interviews, each patient completed a comprehensive questionnaire that was composed of 5 main sections: (1) basic personal data; (2) factors possibly related to AS (GI or GU infection, physical trauma history which made a patient visit a doctor, intense physical training, heavy work) in the 1 month antecedent to disease onset, and history of military service; (3) family history (relatives within the third degree) of AS and other SpAs, uveitis, psoriasis, inflammatory bowel disease (IBD); (4) disease course (age at disease onset, symptoms, diagnosis and treatment) and extramusculoskeletal manifestations (uveitis, immunoglobulin A [IgA] nephropathy, and colitis diagnosed by specialists); (5) Bath AS indices with a 0–10 cm visual analog scale (VAS),²³ including the Bath AS Disease Activity Index (BASDAI),²⁴ Bath AS Functional Index (BASFI),²⁵ and Bath AS Patient Global Assessment (BAS-G).²⁶

Clinical evaluation

The medical chart of each patient was reviewed. A single rheumatologist performed a thorough physical examination for each subject, including any synovitis or enthesitis, range of motion (ROM) of spine and peripheral joints, and chest expansion. The value measured was then transformed into each item for the Bath AS Metrology Index (BASMI).²⁷ Physician's Global Assessment (PGA) score was evaluated with a 0–10 cm VAS by the rheumatologist.

Laboratory tests

The erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP), and serum IgA are 3 markers that are usually used to evaluate the disease activity of AS. ESR was measured with the Westergren method. Serum CRP and IgA levels were measured by nephelometry. The 3 indices were measured on the day of the interview (present value). We also retrospectively collected the values of the 3 indices recorded in the medical chart on the 1st day of visit to our hospital for AS (initial value) and the highest values during the entire clinical course (peak value). In addition, HLA-B27 typing was done by flow cytometry.

Radiography

Conventional plain films were used to assess disease severity. Each film was evaluated by 1 radiologist and

1 rheumatologist (not the one performing physical examination). If there was a discrepancy, the 2 specialists discussed and gave a conclusive grade or score. The sacroiliac joint (SIJ) was graded as 1–4 with anteroposterior pelvis view. Lateral views of the cervical and lumbar spine were taken to score the modified Stoke AS Spinal Score (mSASSS).²⁸ Hip arthritis was evaluated with anteroposterior and lateral views of the hip joints.

Statistical analysis

The comparisons between JAS and AAS groups were carried out using χ^2 test or Fisher's exact test for categorical variables, and Mann-Whitney U test or *t* test for continuous variables as appropriate. A value of *p* < 0.05 was considered statistically significant. Statistical analyses were performed with SPSS version 14.0 (SPSS Inc., Chicago, IL, USA).

Results

There were 169 AS patients (47 JAS, 122 AAS) included in our study. The demographic data are shown in Table 1. The gender distribution was similar for the 2 groups. The mean age of the JAS patients was significantly younger than that of the AAS patients (26.9 ± 9.6 vs. 37.3 ± 11.7 years). A substantial proportion of our patients (40.4% of JAS, 34.4% of AAS) had physical trauma history in the 1 month before disease onset. Additionally, 22.7% of JAS patients had intense physical

training, while 25.2% of AAS patients had heavy work during the period. About half of the patients, in both JAS and AAS groups, had family histories (relatives within the third degree) of AS.

As Table 1 shows, the onset ages were 12.8 ± 2.7 and 25.0 ± 7.4 years for the JAS and AAS groups, respectively. The disease duration was similar in the 2 groups (14.1 ± 9.7 years in JAS vs. 12.5 ± 9.5 years in AAS), as were the years of delay in diagnosis (5.7 ± 6.3 years for JAS vs. 4.6 ± 6.8 years for AAS). The comparisons of clinical manifestations of JAS and AAS patients are shown in Table 2. We divided the symptoms into 3 types: axial symptoms (including spine and SIJ), peripheral enthesopathies, and peripheral arthritis. The 2 groups had obvious differences in initial symptoms, i.e. mainly peripheral enthesopathies and arthritis in JAS patients, and mainly axial symptoms in AAS patients (*p* < 0.001). In detail, the first involved areas were pelvic entheses (23.9%), heel entheses (23.9%), knee joints (19.6%), and hip joints (17.4%) in the JAS group; while 57.8% of AAS patients initially presented with lumbar spine or SIJ pain. Also, the 2 groups had diverse clinical courses during similar disease durations. All but 1 of the JAS patients had some enthesopathies on any occasion. They had significantly higher prevalence for pelvic and heel enthesopathies, and hip and knee arthritis, than AAS patients. As to extramusculoskeletal involvement, an interesting finding was noted that a higher percentage of JAS patients had uveitis, IgA nephropathy (IgAN), or colitis, but the difference was significant only in IgAN.

Table 1. Demographic characteristics of juvenile-onset and adult-onset ankylosing spondylitis patients*

	Juvenile-onset AS (n=47)	Adult-onset AS (n=122)	<i>p</i> [†]
Male	41 (87.2)	101 (82.8)	0.480
Age (yr)	26.9±9.6 (9–51)	37.3±11.7 (19–69)	<0.001
Age at AS onset (yr)	12.8±2.7 (5–16)	25.0±7.4 (17–53)	<0.001
Duration of AS (yr)	14.1±9.7 (1–39)	12.5±9.5 (0–46)	0.330
Delay in diagnosis (yr)	5.7±6.3 (0–28)	4.6±6.8 (0–46)	0.358
Factors possibly related to AS [‡]			
GI or GU infection	6 (12.8)	12 (9.8)	0.580
Physical trauma	19 (40.4)	42 (34.4)	0.467
Intense physical training [§]	11 (22.7)	12 (10.1)	0.021
Heavy worker	2 (4.3)	34 (25.2)	<0.001
Family history of AS	24 (51.1)	62 (50.8)	0.977
Family history of other SpAs, uveitis, IBD, psoriasis	0 (0.0)	4 (3.3)	0.268

*Data presented as n (%) for categorical variables and mean ± standard deviation (range) for continuous variables; [†]statistical significance if *p* < 0.05, comparisons performed with χ^2 or Fisher's exact test for categorical variables and *t* test for continuous variables; [‡]histories of these factors in the 1 month prior to AS onset; [§]intense physical training defined as a team player receiving strict and high amount of physical training; ^{||}heavy worker defined as a worker doing heavy labor, such as a house builder, painter, porter. AS = ankylosing spondylitis; GI = gastrointestinal; GU = genitourinary; SpAs = spondyloarthropathies; IBD = inflammatory bowel disease.

Table 2. Comparison of clinical manifestations of juvenile-onset and adult-onset ankylosing spondylitis (AS) patients*

	Juvenile-onset AS (n = 47)	Adult-onset AS (n = 122)	p [†]
Initial symptoms			< 0.001
Axial symptoms (including spinal and sacroiliac joint)	2 (4.3)	82 (66.9)	
Peripheral enthesopathy	28 (58.7)	23 (19.0)	
Peripheral arthritis	17 (37.0)	17 (14.0)	
Clinical symptoms at any time of disease			
Low back pain	42 (89.4)	118 (96.7)	0.069
Middle back pain	22 (46.8)	73 (59.8)	0.126
Upper back pain	32 (68.1)	77 (63.1)	0.545
Any peripheral enthesopathy	46 (97.9)	88 (72.1)	< 0.001
Pelvic enthesopathy [‡]	34 (72.3)	54 (44.3)	< 0.001
Knee enthesopathy [§]	14 (29.8)	24 (19.7)	0.158
Heel enthesopathy	26 (55.3)	24 (19.7)	< 0.001
Costosternal enthesopathy	16 (34.0)	50 (41.0)	0.407
Sausage digit	2 (4.3)	4 (3.3)	0.534
Any peripheral arthritis	37 (78.7)	55 (45.1)	< 0.001
Hip joint	29 (61.7)	48 (39.3)	0.009
Knee joint	18 (38.3)	17 (13.9)	0.006
Foot (including ankle, tarsal, and toe arthritis)	11 (23.4)	14 (11.5)	0.050
Shoulder joint	6 (12.8)	13 (10.7)	0.697
Elbow joint	3 (6.4)	4 (3.3)	0.302
Hand joint (including wrist, carpal, and finger arthritis)	7 (14.9)	12 (9.8)	0.351
Temporomandibular joint	1 (2.1)	4 (3.3)	0.573
Extramusculoskeletal involvement			
Uveitis	17 (36.2)	27 (22.1)	0.062
IgA nephropathy	7 (14.0)	5 (3.7)	0.014
Colitis	4 (8.5)	7 (5.7)	0.501

*Data presented as n (%); [†]statistical significance if $p < 0.05$, comparisons performed with χ^2 or Fisher's exact test; [‡]pelvic enthesopathy, including enthesitis over the iliac crest, anterior and posterior superior iliac spine, greater trochanter, ischial tuberosity, and pubis symphysis; [§]knee enthesopathy, including patellar enthesitis and quadriceps enthesitis; ^{||}heel enthesopathy, including Achilles enthesitis, plantar fasciitis, and tibialis posterior enthesitis.

Table 3. Bath ankylosing spondylitis indices and clinical evaluation of juvenile-onset versus adult-onset ankylosing spondylitis (AS) patients*

	Juvenile-onset AS (n = 47)	Adult-onset AS (n = 122)	p [†]	p [‡]
BASDAI (0–10)	3.84 ± 1.90	3.33 ± 1.89	0.108	0.598
BASFI (0–10)	1.81 ± 1.71	1.80 ± 1.86	0.941	0.529
BAS-G (0–10)	3.60 ± 2.25	3.54 ± 2.53	0.875	0.393
BASMI (0–10)	1.95 ± 2.16	1.64 ± 2.29	0.298	0.264
Chest expansion (cm)	5.35 ± 2.32	5.48 ± 2.06	0.682	0.118
PGA score (0–10)	2.40 ± 1.33	2.07 ± 1.09	0.152	0.610

*Measures were performed on the day of interview and data are presented as mean ± standard deviation; [†]statistical significance if $p < 0.05$, comparisons performed with Mann-Whitney U test; [‡]p value after adjustment for age and disease duration. BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath Ankylosing Spondylitis Functional Index; BAS-G = Bath Ankylosing Spondylitis Patient's Global Assessment; BASMI = Bath Ankylosing Spondylitis Metrology Index; PGA = Physician's Global Assessment.

The Bath AS indices and PGA score are listed in Table 3. A trend was noted that BASDAI, BASMI and PGA scores were higher in JAS patients, but only significantly in the peripheral joint item of BASDAI ($p = 0.010$) after adjustment for age and disease

duration. The BASFI and BAS-G were comparable for the 2 groups. Table 4 shows the laboratory data. More than 97% of our patients had HLA-B27 in both JAS and AAS. The CRP and ESR levels were higher in the JAS than the AAS group except for initial ESR.

Table 4. Laboratory data in juvenile-onset and adult-onset ankylosing spondylitis patients*

	Juvenile-onset AS (n = 47)	Adult-onset AS (n = 122)	p [†]
Positive HLA-B27	46 (97.7)	119 (97.2)	0.691
ESR (mm/hr)			
Initial	31.6 ± 23.5	27.9 ± 25.1	0.167
Peak	44.1 ± 28.9	34.6 ± 27.1	0.031
Present	27.3 ± 20.0	21.5 ± 21.0	0.027
CRP (mg/dL)			
Initial	2.13 ± 2.41	1.13 ± 1.29	0.031
Peak	2.39 ± 2.49	1.37 ± 1.40	0.032
Present	1.82 ± 1.86	0.93 ± 1.06	0.007
IgA (mg/dL)			
Initial	394.7 ± 163.2	360.7 ± 151.7	0.201
Peak	440.3 ± 172.4	393.6 ± 157.4	0.121
Present	382.2 ± 151.5	360.5 ± 140.5	0.356

*Data presented as n (%) for categorical variables and mean ± standard deviation for continuous variables; [†]statistical significance if $p < 0.05$, comparisons performed with Fisher's exact test for positive HLA-B27 and Mann-Whitney U test for others. AS = ankylosing spondylitis; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; IgA = immunoglobulin A.

Table 5. Radiological evaluation of juvenile-onset and adult-onset ankylosing spondylitis patients*

Location	Juvenile-onset AS (n = 47)	Adult-onset AS (n = 122)	p [†]	p [‡]
Sacroiliac joint			0.266	0.463
Grade 0	0 (0)	0 (0)		
Grade 1	0 (0)	0 (0)		
Grade 2	17 (36.2)	52 (42.6)		
Grade 3	8 (17.0)	26 (21.3)		
Grade 4	22 (46.8)	44 (36.1)		
Spine evaluated by mSASSS				
Cervical spine (0–36)	2.74 ± 7.33	6.06 ± 12.13	0.306	0.325
Lumbar spine (0–36)	8.96 ± 9.98	11.59 ± 13.05	0.498	0.687
Sum of cervical and lumbar spine (0–72)	9.58 ± 14.57	15.43 ± 23.43	0.704	0.345
Hip arthritis			0.001	0.012
Bilateral hip arthritis	22 (46.8)	23 (18.9)		
Unilateral hip arthritis	3 (6.4)	5 (4.1)		
No hip arthritis	22 (46.8)	94 (77.0)		

*Data presented as n (%) for categorical variables and mean ± standard deviation for continuous variables; [†]statistical significance if $p < 0.05$, comparisons performed with χ^2 test for categorical variables and Mann-Whitney U test for ordinal and continuous variables; [‡]p value after adjustment for age and disease duration. AS = ankylosing spondylitis; mSASSS = modified Stoke Ankylosing Spondylitis Spinal Score.

A slightly higher, but not significant, IgA in JAS patients was noted.

The radiological evaluations are presented in Table 5. SIJ grading was identical bilaterally in most cases (86.1% of AAS and 85.1% of JAS), and differed by only 1 grade in others. Therefore, we took the severe side as the SIJ grade if the grading was unequal bilaterally. There was no significant discrepancy in SIJ grading and mSASSS in the 2 groups, although there was a trend of higher mSASSS in AAS patients. On the other hand, the radiographic evidence of hip

joint involvement was much more common in the JAS group, especially bilaterally, i.e. bilateral hip involvement in 46.8% of JAS and 18.9% of AAS patients, unilateral hip arthritis in 6.4% of JAS and 4.1% of AAS patients ($p = 0.012$ after adjustment for age and disease duration).

Table 6 lists the therapies that these 169 patients experienced. Most of our AS patients (97.9% of JAS and 95.1% of AAS) had received sulfasalazine treatment. However, more JAS patients had taken methotrexate and systemic (oral or intravenous) steroid than AAS

Table 6. Treatment for juvenile-onset and adult-onset ankylosing spondylitis patients*

Management	Juvenile-onset AS (n = 47)	Adult-onset AS (n = 122)	p [†]
DMARDs			
Sulfasalazine	46 (97.9)	116 (95.1)	0.373
Methotrexate	6 (12.8)	5 (4.1)	0.041
Systemic steroid treatment	22 (46.8)	36 (29.5)	0.034
Antitumor necrosis factor	2 (4.3)	2 (1.6)	0.309
Symptomatic treatment (in recent 1 mo)			
NSAIDs	44 (93.6)	101 (82.8)	0.053
Muscle relaxant	22 (46.8)	56 (45.9)	0.916
Acetaminophen	3 (6.4)	9 (7.4)	0.560
Anxiolytic agents	2 (4.3)	11 (9.0)	0.244
Total hip replacement	5 (10.6)	4 (3.3)	0.069
Spinal correction surgery	0 (0.0)	3 (2.5)	0.374

*Data presented as n (%); †statistical significance if $p < 0.05$, comparisons performed with χ^2 or Fisher's exact test. DMARDs = disease-modifying antirheumatic drugs; NSAIDs = nonsteroidal anti-inflammatory drugs.

patients. There were only a few patients (2 JAS, 2 AAS) who had received anti-TNF therapy, due to lack of reimbursement from the Taiwan National Health Insurance. The symptomatic remedies in the 1 month before the interviewing day, including NSAIDs, muscle relaxants, acetaminophen, and anxiolytic agents, were used similarly in the 2 groups. The 2 most common operations in AS patients—total hip replacement and spinal correction—were not significantly different between the 2 groups.

Discussion

This is the first study that comprehensively compared the disease course of JAS and AAS patients in the Taiwan population. In the present study, we noted many remarkable differences between the 2 groups, including possible risk factors, clinical pictures, inflammatory markers, and radiographic evidence of hip arthritis. However, there were no obvious disparities in gender distribution, family history of AS, functional limitations, most of the Bath AS indices, and radiographic scoring of axial joints.

In our 169 AS patients, the male-to-female ratio was 4.8 for the AAS group and 6.8 for the JAS group, which is higher than the ratio of 2–3 found in other series from Western countries.^{29,30} We investigated the prevalence of possible risk factors for AS. A rather high percentage (around 50%) of our patients, regardless of being in the JAS or AAS group, had a family history of AS. This might be because a patient with familial AS would seek medical resources more readily. Also, we found a substantial prevalence of preceding GI/GU infection and physical trauma for both JAS and AAS

patients. More intense physical training in the JAS group and more heavy working in the AAS group before the onset of AS were noted. To date, it has not been studied whether the 2 factors are connected with the onset of AS. We suspect that both of them could produce repeat microtrauma, which acts like physical trauma and may facilitate the development of AS. Moreover, we noticed that 56.4% of AAS male patients had started to have discomfort or progressive symptoms during or just after being demobilized from military service, an obligation for all Taiwanese male citizens (not shown in table). Although most of these people fell ill in their 3rd decade of life, the most common age of AS onset, we doubt that the intense physical training and infection from poor hygiene in the army promoted the development of AS. Consequently, it is worth studying the link between physical trauma or GI/GU infection in the army and AS.

In the comparison of the clinical manifestations of JAS and AAS patients, we noted that there was no difference between the 2 groups in the number of years of delay in diagnosis ($p = 0.358$), which was contrary to the finding of a longer delay in diagnosis of JAS patients than AAS patients in Stone et al's study (15.3 ± 0.79 years for JAS *vs.* 7.6 ± 0.20 years for AAS, $p < 0.001$).⁴ The cause of earlier diagnosis in our patients as compared with Stone et al's might be due to different sources of patients. Our patients were from the rheumatology clinic of a tertiary medical center, to which patients can have direct access without referral, while their patients were from the register of the Spondylitis Association of America, a support group for spondylitis. As for the symptoms at disease onset, our JAS patients presented with more peripheral enthesitis and peripheral arthritis than

axial symptoms, while most of the AAS patients presented with axial symptoms. During the similar disease duration, much more peripheral enthesopathy (especially in the pelvis and heel), and arthritis of the hip and knee were noted in JAS than in AAS patients. Aggarwal et al found similar patterns of onset symptoms and peripheral joint involvement in JAS patients, but the incidence of enthesitis was comparable in JAS and AAS groups.³¹ Additionally, the prevalence of enthesitis in our patients (97.9% in JAS, 72.1% in AAS) was much higher than that in Aggarwal et al's patients (40% in JAS, 37.3% in AAS). The discrepancy might be due to us reviewing patients' medical charts and conducting face-to-face interviews in our study, by which we could acquire more information about patients' symptoms.

There was an interesting finding of extramusculoskeletal involvement in our study. The JAS group had trends of more uveitis, IgAN, and colitis than the AAS group, although the difference was significant only for IgAN. Although the JAS group had slightly but not significantly higher IgA levels, we did find higher initial and peak IgA in patients with IgAN compared to those without IgAN ($p = 0.042, 0.043, 0.389$ for initial, peak, and present IgA, respectively, not shown in table). Previous studies noted that around half of the patients with IgAN had elevated serum IgA level,³² and the serum undergalactosylated IgA1 played a critical role in this disease.³³ It would be interesting to search for the role of IgA in the pathogenesis of JAS and IgAN in the future. On the other hand, the contingency coefficient between uveitis and peripheral arthritis in our AS patients was 0.155 ($p = 0.041$). The results correlate to those of previous studies.^{34,35} A matching prevalence was found between peripheral arthritis and anterior uveitis, and HLA-linked LMP2 gene was involved in the pathogenesis.^{34,35} Therefore, further studies of the relation between peripheral arthritis and extramusculoskeletal manifestations are expected.

An extensive comparison of several Bath AS indices between the JAS and AAS groups was a conspicuous characteristic in our study. We found that the functional impairment in JAS was nearly the same as that in AAS. This was different from the study of Stone et al,⁴ in which JAS had significantly more functional impairment than AAS. In addition, our study revealed notably higher CRP and ESR in the JAS group. On the basis of more radiographic evidence of hip involvement but not axial joints in JAS patients, we deduced that peripheral joint involvement correlated with elevated inflammatory markers more than axial involvement.

In conclusion, AS tended to arise as peripheral enthesitis or arthritis in JAS patients, while it arose from axial joints in AAS patients. After similar disease duration, there was significantly more radiographic evidence of hip arthritis in JAS, compared with mildly higher (but not significant) mSASSS in AAS. We suspect that JAS and AAS are different disease entities. The modified New York criteria may be insufficient for early diagnosis of JAS because the SIJ is usually intact in the first few years of the course. In addition, the functional outcome was not more impaired in the JAS group than the AAS group in our study. Therefore, timely diagnosis and treatment of JAS are very important. There are some limitations in our study. As a retrospective study, we acquired most data from the medical charts and recollections of our patients. Furthermore, all of the subjects being from a tertiary medical center would lead to some biases. In future studies, we recommend larger-scale case-control or cohort studies to search for the genetics and pathogenesis of JAS.

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