Pattern of Disease Onset, Diagnostic Delay, and Clinical Features in Juvenile Onset and Adult Onset Ankylosing Spondylitis

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ABSTRACT. ***Objective.*** To assess the frequency of juvenile onset ankylosing spondylitis (JOAS) in Turkish patients with AS and to compare with adult onset AS (AOAS) in a cross-sectional study design.

Methods. A total of 322 patients were recruited from the joint database of 5 university hospitals in eastern Turkey.

Results. Patients with JOAS (n = 43, 13.4%) had significantly longer diagnostic delay (9.21 vs 5.08 yrs), less severe axial involvement and more prevalent uveitis (OR 2.92, 95% CI 1.25–6.79), and peripheral involvement at onset (OR 3.25, 95% CI 1.51–6.98, adjusted for current age; and OR 2.26, 95% CI 1.07–4.76, adjusted for disease duration). Patients with AOAS had higher radiographic scores and more restricted clinimetrics but similar functional limitations and quality of life.

Conclusion. JOAS and AOAS had distinctive courses and Turkish patients with AS had similar features compared to other Caucasian patient populations. (First Release Nov 1 2009; J Rheumatol 2009;36:2830–3; doi:10.3899/jrheum.090435)

Key Indexing Terms:
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Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the sacroiliac joints and is characterized by restricted spinal mobility. Disease may be accompanied by peripheral joint symptoms and enthesitis or extraarticular involvement such as uveitis. When preceding symptoms occur in individuals ≤ 16 years of age and followed by radiographic sacroiliitis in later stages, the disease is termed juvenile onset AS (JOAS)[1]. JOAS differs from its counterpart, adult onset AS (AOAS), with clinical features and pattern at onset of high prevalence of peripheral expression and low prevalence of axial involvement[2-4].

We assessed the frequency of JOAS in Turkish patients with AS and determined the differences in clinical and radiological data and delay to diagnosis in JOAS versus AOAS.

MATERIALS AND METHODS

Patients were recruited from the joint database of rheumatology clinics of 5 university hospitals located in the eastern part of Turkey. This database is composed of patients who met the modified New York criteria for AS[5], who were attending these tertiary centers and were consecutively included between October 2006 and October 2008.

Patients were evaluated using a standard examination and assessment protocol, which was adopted at 3 meetings of study investigators from these centers held in 2006. Clinical features, age at symptom onset, age at diagnosis, and family history for spondyloarthropathies (SpA) were recorded. The pattern of disease onset was assessed by asking patients for

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the first symptom and/or manifestation related to their disease. Symptoms at disease onset were classified in 2 categories in accord with the ASAS definitions[6] as follows: (1) an axial pattern, axial manifestations (including inflammatory back pain) with or without peripheral manifestations; and (2) a peripheral pattern, with individual manifestations, i.e., an extraaxial sign or symptom of AS, such as peripheral arthritis and enthesitis, and also associated diseases belonging to the spondyloarthritides, such as acute anterior uveitis (AAU) or inflammatory bowel disease (IBD) and psoriasis. Current or previous history for AAU, IBD, and psoriasis were recorded. Patients were examined for current arthritis (swelling and tenderness of peripheral joints) and enthesitis. Delay of diagnosis was defined as the time elapsed between onset of first symptoms and diagnosis by a healthcare provider. Patients were questioned for their medications and examined for anthropometric measurements. The Bath AS Metrology Index[7] was used to grade the mobility of the spine and hip on a scale of 0–10.

Patients aged < 18 years were excluded from the analysis. Patients with disease-related symptom onset at age ≤ 16 years were classified as having JOAS and those with onset at age > 17 were classified as having AOAS. All patients were informed of the study protocol and gave their written informed consent.

The Bath AS Disease Activity Index[8] was used to assess disease activity. The Bath AS Functional Index[9] was used to assess functional status. Disease-related quality of life was measured with the AS Quality of Life Scale[10].

All radiographs, with patients' identity removed, were scored by the same rheumatologist (SO) in the study coordinating center, using the New York criteria, Bath Ankylosing Spondylitis Radiographic Index (BASRI; BASRI-spine and BASRI-hip), and Stoke Ankylosing Spondylitis Spine Score (SASSS and modified-SASSS).

Statistic analysis. For comparison of JOAS and AOAS we calculated the odds ratio (OR) and 95% confidence intervals (95% CI) for each study characteristic adjusted by current age or disease duration in a binary logistic regression model. A 2-tailed p value < 0.05 was considered significant. Analyses were performed using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 322 patients aged 18–72 years out of 334 in the institutional database who met the modified New York Criteria[5] for AS were included. Forty-three had JOAS (13.4%) and there was no gender difference between the groups. Patients' characteristics, functional limitations, quality of life, disease activity, history, type of disease onset, and extraarticular manifestations are described in Table 1.

Patients with JOAS had better values in some of the clinimetric indicators (Table 2). Patients with JOAS were more likely to have lesser severity of axial radiographic changes as assessed by SASSS, mSASSS, and BASRI-spine scores (Table 2).

DISCUSSION

This is the first study comparing Turkish patients with JOAS and AOAS in a large population; we observed that patients with JOAS experience a greater delay to diagnosis and less severe axial symptoms and radiographic involvement, after controling for disease duration. Patients with JOAS are also more likely to have peripheral arthritis. There was a trend in patients with JOAS for having more peripheral pattern disease at disease onset compared to AOAS, and also increased risk for having uveitis (adjusted for current age).

The prevalence of JOAS in Turkish patients was 13.4%, similar to reports in Caucasian populations (9%–21%), although higher prevalences have been reported for Mexican Mestizos and Korean patients[2,3].

Delay to diagnosis, regardless of age at symptom onset, was nearly 5.6 years in our study population. In previous studies similar to ours, longer delays to diagnosis in patients with JOAS compared to AOAS have been reported[4,11].

Patients with JOAS have been suggested to have worse functional outcome compared to those with AOAS[11]; however, conflicting results have been reported by others[4,12-15]. In a well designed study, O'Shea, *et al* reported worse functional outcome and quality of life measures in AOAS compared to JOAS[14]. On the other hand, Gensler, *et al* reported similar functional outcomes in adult onset compared to juvenile onset AS[13].

There is a tendency for more severe axial involvement in AOAS compared to JOAS. Gensler, *et al* reported that AOAS patients had more severe BASRI-spine scores, after adjustment for multiple covariates[13]. Similar observations were reported in a recent study by O'Shea, *et al*[14]. Additionally, similar percentages of radiographic evidence for hip involvement were reported by these authors[14]. In our study, there was a trend for higher BASRI-hip scores in patients with JOAS, but this was not statistically significant. Gensler, *et al* reported more severe hip involvement in JOAS patients using the BASRI-hip[13]. We used 3 radiographic scoring methods, and found that all these systems worked well documenting radiographic severity in JOAS and AOAS.

In our study patients with JOAS were more likely to have uveitis or history of uveitis compared to patients with AOAS, in accord with previous reports[2,14]. Additionally, in accord with previous reports, JOAS patients were more likely to have a peripheral disease pattern at disease onset[11,14,16].

Regarding the clinimetric or anthropometric measures, we found significant differences between JOAS and AOAS in cervical rotation and lateral flexion measurements after adjusting for disease duration, indicating a more severe axial involvement in AOAS. Similar observations were noted by O'Shea, *et al*, who found much more restricted cervical rotation and lateral flexion in patients with AOAS[14].

Our study has some limitations. First, patients were recruited from the joint database of tertiary care centers and it is difficult to say that the study population reflects all patients with AS in the general population. Second, questioning patients for date of symptom onset may introduce recall bias. However, all the patient-reported outcome measurements or patient histories bear the risk for recall bias in various degrees.

Our study of Turkish patients with AS had quite similar results compared to studies conducted in different AS populations. There was a longer delay to diagnosis of JOAS, and

Table 1. Characteristics of patients with adult onset AS (AOAS) (n = 279) and juvenile onset AS (JOAS) (n = 43).

Characteristic	AOAS Mean	AOAS SD	AOAS Median	JOAS Mean	JOAS SD	JOAS Median
Current age, yrs†	36.11	10.20	35	29.33	8.01	28
Height, cm	169.50	8.60	170	170.80	9.10	172
Weight, kg	71.80	14.20	70	67.20	12.20	66
Age at symptom onset, yrs †	25.63	7.49	24	12.67	2.90	13
Age at diagnosis, yrs†	30.70	9.42	29	21.79	5.22	22
Delay in diagnosis, yrs†	5.08	5.99	3	9.21	5.41	9
Disease duration, yrs†	10.49	8.16	8	16.81	7.88	15
Mean BASDAI††	4.06	2.44	3.9	4.06	2.53	4.0
BASDAI-fatigue††	5.23	3.42	5	5.36	2.94	6
BASDAI-enthesitis††	3.61	3.41	2.5	4.06	3.68	3
ASQOL††	9.41	6.04	10	9.82	5.53	12
BASFI††	38.73	28.73	37.2	40.57	28.43	41.1
Gender, M/F	226/53			39/4		
BASFI > 50, %††	37.1			38.1		
Marital status, %						
Married	69.3			54.8		
Single	25.6			40.4		
Divorced/widow	4.0			2.4		
Living with partner	1.1			2.4		
Smoking, %						
Never/ex-smoker	48.7			51.2		
Smoker	51.3			48.8		
Education, %						
High school or less	69.9			69.8		
University or more	30.1			30.2		
Positive family history for SpA, %††	26.7			31.6		
Positive family history for AS, %††	20.7			26.3		
Positive history for psoriasis, %††	6.2			2.4		
Positive history for urethritis, %††	11.2			7.9		
Positive history for inflammatory bowel disease, %††	4.0			7.9		
Current arthritis, %*	26.2			41.5		
Uveitis/positive history for uveitis, %**	10.9			23.3		
Only peripheral pattern at disease onset, %***	15.1			32.6		

† $p < 0.001$, t test, JOAS vs AOAS. †† No significant odds ratio even after adjustment for current age or disease duration. * Unadjusted odds ratio 1.99 (95% CI 1.01–3.93). ** Age adjusted odds ratio 2.92 (95% CI 1.25–6.79). *** Age adjusted odds ratio 3.25 (95% CI 1.51–6.98), disease duration adjusted odds ratio 2.26 (95% CI 1.07–4.76). BASDAI: Bath AS Disease Activity Index; BASFI: Bath AS Functional Index; ASQOL: AS Quality of Life Index; SpA: spondyloarthropathy.

Table 2. Anthropometric measurements and radiographic scoring of the juvenile onset (JOAS) and adult onset ankylosing spondylitis (AOAS) patients.

Measure	AOAS Mean	AOAS SD	AOAS Median	JOAS Mean	JOAS SD	JOAS Median	OR (95% CI) Adjusted for Age	OR (95% CI) Adjusted for Disease Duration
Cervical rotation (°)	56.47	25.15	60.00	63.94	21.35	70.00	1.00 (0.99–1.02)	1.03 (1.01–1.04)*
Tragus-to-wall, cm	16.86	7.04	15.00	16.55	6.99	14.75	1.04 (0.99–1.09)	0.94 (0.88–1.00)
Lateral flexion, cm	9.95	5.76	9.50	10.34	5.99	10.00	0.95 (0.89–1.01)	1.08 (1.01–1.15)*
Schober, cm	3.10	1.95	3.00	2.93	2.09	2.25	0.86 (0.72–1.04)	1.07 (0.90–1.29)
Intermalleolar distance, cm	96.17	28.43	100.00	95.29	32.32	97.00	0.99 (0.98–1.00)	1.00 (0.99–1.02)
BASMI	3.53	2.61	3.00	3.10	2.55	3.00	1.07 (0.93–1.24)	0.78 (0.66–0.92)*
Chest expansion, cm	3.99	1.94	4.00	4.18	1.92	4.00	0.90 (0.75–1.09)	1.20 (1.00–1.45)*
Finger-to-floor, cm	22.13	15.94	22.00	22.25	16.71	19.25	1.00 (0.98–1.03)	0.98 (0.96–1.00)
mSASSS	27.09	17.42	23.00	21.96	14.65	19.00		1.08 (1.04–1.12)*
SASSS	24.13	18.69	18.50	21.51	18.14	19.00		1.04 (1.01–1.07)
BASRI-spine	7.99	2.19	7.50	7.56	2.05	7.00		1.43 (1.10–1.86)*
BASRI-hip	0.84	0.87	1.00	1.28	1.25	1.00		0.86 (0.58–1.28)

* Statistically significant.

one would not expect classical inflammatory back pain as a presenting symptom in juvenile patients. Further studies, particularly comprising prospective followup of patients, could lead to better understanding of phenotypic differences and prognostic factors between JOAS and AOAS.

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