Demographic, clinical, and laboratory features of Turkish patients with late onset ankylosing spondylitis

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ABSTRACT

Ankylosing spondylitis (AS) is a chronic inflammatory disease, which typically begins in early decades of life with primarily axial joints involvement. This disease rarely affects patients older than 50 years of age. The aim of this study was to compare and evaluate the demographic, clinical, and laboratory features of late onset and early onset AS patients who were followed up in a single rheumatology center. A total of 339 patients who have been diagnosed with AS according to modified New York criteria were included in the study. The patients whose initial symptoms were observed after 50 years of age were accepted as late onset AS. Out of 339 patients, 27 (7.9%) were diagnosed as late onset AS and 312 (92.3%) patients were evaluated as early onset AS. Of 27 late onset patients, 10 were male and 17 were female. Delay in the diagnosis was 5.8 years for early onset AS, while it was 3.8 years for late onset AS (p = 0.001). Higher levels of acute phase reactants and more methotrexate (MTX) use were detected in early onset AS patients compared to late onset AS (p = 0.001, p = 0.007, respectively). Statistically, there was no difference between these two groups, with regard to disease clinical activity indexes, anthropometric measurement parameters, uveitis and peripheral joint involvement. In this study, we showed that early and late onset AS patients may present with different clinical, genetic, and laboratory features. Late onset AS patients are characterized with lower human leukocyte antigen-B27 sequence, less inflammatory sign, delayed diagnosis, and less MTX and anti-tumor necrosis factor alpha drug usage.

KEYWORDS: Ankylosing spondylitis; late onset; features; Turkey
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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease characterized by axial and peripheral joint involvement [1]. It usually affects young male population [2]. The course of the disease is different in women than in men [3]. As for the patients over the age of 50, initial symptoms of AS are rarely seen. The incidence of early onset AS has been determined as 7.7/100,000 per year and the incidence of late onset AS as 2.2/100,000 per year in a previous study [4]. According to the records of German Corporation of AS; the cases of AS with an onset over 40 years of age were reported to be 6% of all cases and most of these were human leukocyte antigen (HLA)-B27 negative [5]. In another French study, 70% of late onset AS patients were determined to be HLA-B27 positive [6]. The obvious fact is that the late onset AS cases are different than the early onset AS cases in terms of clinical appearance, radiological, and laboratory features. Late onset AS is a more severe disease, characterized with elevated plasma inflammatory markers, more involvement of cervical, and peripheral joints, as compared to early onset form of the disease [7,8]. Some of the late onset AS cases can even present with clinical features similar to that of polymyalgia rheumatic (PMR), sarcoidosis or reflex sympathetic dystrophia [9-11]. Eventually the fact must be kept in mind that sometimes patients who had spinal symptoms in their early lives may be diagnosed as AS in the older ages.

The aim of our study was to compare the demographic, clinical, radiological, and laboratory features of late and early onset AS patients and to demonstrate the probable differences among these patients.

MATERIALS AND METHODS

We included 339 patients in this study, who were followed up by a single rheumatology center and diagnosed with AS

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according to modified New York classification criteria [12]. The patients who had initial symptoms started after 50 years of age were accepted as late onset AS. All of the patients were divided into two groups as late onset and early onset and were compared in terms of: (1) epidemiological data (age, duration of disease, delay in diagnosis, smoking habit); (2) gender, HLA-B27; (3) clinical features (initial symptom, clinical form, extra articular involvement, etc.); (4) physical examination and anthropometric measurements (chest expansion, Schober test, hand-to-floor distance, occiput-to-wall distance); (5) disease activity parameters (Bath AS disease activity index [BASDAI], Bath AS functional index [BASFI]); and (6) drug usage. Detailed history of all the patients were taken, systemic and musculoskeletal system examinations were performed, laboratory tests like erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, and HLA-B27 were implemented. Joint involvements were evaluated by radiological imaging (conventional radiography and magnetic resonance imaging). Presence of an active or past uveitis was investigated by an ophthalmologist.

Statistics

Data was analyzed by statistical package for the social sciences (SPSS) 20.0 software for Windows statistical package (SPSS, Chicago, Illinois, USA). Categorized data was cross tabled and tested with Chi-square test. Numeric variables, which change in normal ranges were analyzed with *t*-test, abnormally ranged variables were analyzed with Mann-Whitney-U test. Pearson correlation coefficients for variables with normal distribution were used. Statistical significance threshold value was 0.05.

RESULTS

A total of 339 AS patients were included in this study. Of these 339 patients, 312 (92.3%) were early onset AS, 27 (7.9%) were late onset AS. Of 27 late onset AS patients, 10 were male and 17 were female. Mean patient age was 38.7 years for early onset group and 62.1 years for late onset group. Mean duration of disease was 8.9 years for early onset group and 2.3 years for late onset group (p = 0.001). Delay in diagnosis was 5.8 years for early onset group and 3.8 years for late onset group (p = 0.001). Smoking habit was determined to be more common in early onset group, but this was not statistically significant (p = 0.260). Higher levels of acute phase reactants (CRP, ESR) were determined in the early onset group as compared to late onset group (p = 0.001). There was no significant difference in terms of disease activity indexes (BASDAI, BASFI) and measurement parameters (Schober, chest expansion etc.). Enthesitis was seen in 92% of the early onset AS cases and in all the late onset AS cases. Upon comparison in terms of extra articular involvement, the incidence rate of uveitis was also similar for both groups (p = 0.615). In a comparison of the peripheral joint involvement, there was no statistically significant difference (p = 0.879). In the evaluation of genetics tests, we found more frequent HLA-B27 positivity in early onset AS group (p = 0.03). In terms of the treatment options chosen, there was no significant difference in the use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CS), and sulfasalazine, but there was a more frequent use of methotrexate (MTX) in early onset AS group (p = 0.007). More frequent anti-tumor necrosis factor (TNF)-alpha usage was detected in early onset AS patients, but this difference wasn't statistically significant (Table 1).

DISCUSSION

In this study, we showed that early and late onset AS patients can present with different clinical, laboratory, and genetic features. According to our results, late onset AS patients were characterized with lower frequency of HLA-B27 positivity, lower levels of inflammatory markers, delay in diagnosis and less use of MTX and anti-TNF-alpha. In our study, we set the late onset criteria as being older than 50 years of age, unlike some other studies. In addition, our study included only the patients diagnosed with AS, but none of

TABLE 1. Demographic, clinical and laboratory features of early versus late onset AS patients

Features	Early AS (N=312)	Late AS (N=27)	*p*-value
Male (%)	174 (55.8)	10 (37.3)	0.001
Mean patient age (year)	38.7	62.1	
Mean disease duration (year)	8.9	8.3	0.001
Delay of the diagnosis (year)	5.8	3.8	0.001
Peripheral arthritis (%)	103 (33)	10 (8.8)	0.879
Cervical involvement (%)	217 (69.6)	20 (74.1)	0.402
Uveitis (%)	55 (17.6)	6 (22.2)	0.615
HLA-B27 positivity (%)	190 (60.9)	11 (40.7)	0.003
Smoking status (%)	165 (52.9)	12 (44.4)	0.260
BASDAI (cm)	5	4.9	0.213
BASFI (cm)	3.7	3.9	0.160
Hand to floor distance (cm)	10.9	10.7	0.483
Chest expansion (cm)	3.9	3.6	0.859
Schober test (cm)	4.5	4.0	0.603
CRP (mg/dl)	3.9	0.8	0.001
ESR (mm/h)	27.9	17.2	0.001
SSZ (%)	249 (79.8)	23 (85.2)	0.351
MTX (%)	54 (17.3)	0 (0)	0.007
CS (%)	58 (18.6)	4 (14.8)	0.428
NSAIDs (%)	304 (97.4)	25 (92.6)	0.185
Anti-TNF-alpha (%)	34 (10.9)	1 (3.7)	0.260

AS: Ankylosing spondylitis; HLA: Human leukocyte antigen; BASDAI: Bath AS disease activity index; BASFI: Bath AS functional index; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; SSZ: Sulfasalazine; MTX: Methotrexate; CS: Corticosteroids; NSAIDs: Non-steroidal anti-inflammatory drugs; TNF: Tumor necrosis factor

the other spondyloarthritis (SpA) subgroups. We determined lower HLA-B27 positivity and lower levels of inflammatory markers in the late onset AS group, which was not compatible with the results of previous studies. This contradiction may be explained by the heterogenecity of the patient population included in previous studies. In addition, delay in diagnosis was determined less in our late onset AS group. This may be explained by recent improvements in diagnostic options (laboratory, radiology, and scintigraphy) and growing experience in this group of diseases. Furthermore in our study, we determined less usage of MTX and anti-TNF-alpha in late onset AS group.

AS is a chronic inflammatory disease which starts usually in the second or third decades of life and is the prototype of the SpA. Clinical findings rarely appear after 50 years of age and therefore it's not a primarily considered diagnosis [13]. In comparison to common rheumatologic pathologies at this age (i.e. PMR, rheumatoid arthritis, RS3PO), late onset AS is generally a missed clinical condition and it is usually not considered hence late diagnosed [14]. The main reason for this may be the differences in clinical appearance of the disease in older patients.

When we reviewed previous studies regarding late onset SpA, we found several case reports and comparative studies. These studies were too diversified and unreliable because they mostly included small patient series, different subgroups of rheumatologic diseases and different cut-off age values for determining "late-onset." Dubost and Sauvezie have shared their experience about clinical features often late-onset peripheral SpA patients [15]. All of these patients were male with mild axial involvement, apparent severe constitutional symptoms, oligoarthritis, pitting edema, elevated inflammatory parameters, and HLA-B27 positivity. These patients were generally characterized with poor responses to NSAIDs. In another study, Caplanne et al. have compared late onset SpA patients with early onset SpA patients [16]. They have reported more frequent neck and back pain, chest involvement, peripheral arthritis and systemic involvement in late onset cases and compared with early onset SpA cases. Mild response was obtained to NSAIDs treatment in these patients. Olivieri et al. have shown that the disease had a large clinical spectrum after their 5-year follow-up of 23 late onset SpA cases [17]. They have reported pitting edema in three cases and elevated levels of inflammatory markers in many cases in addition to the classical symptoms of the disease (low back pain, peripheral arthritis, enthesitis, dactylitis). Kay et al. have shared their experience about 228 late onset SpA cases [18]. According to their study that they compared late onset SpA patients with early onset patients, higher rates of cervical involvement and peripheral arthritis were determined as the characteristics of late onset SpA. Montilla et al. have inspected 1257 AS cases from the records of Spanish Rheumatology Association retrospectively and found out that 44 of them (3.5%) had initial symptoms after 50 years of age [19]. They reported more frequent peripheral arthritis, cervical, and cardiac involvement but less frequent uveitis in late onset AS cases compared to early onset AS. Although there is some information and some studies about late onset SpA in general, there is still too little data available on the late onset AS patients. AS, which is a prototype of these diseases, would provide a more homogeneous group of late onset patients.

We must consider the differential diagnosis of the late onset AS than other inflammatory rheumatologic pathologies and paraneoplastic syndromes. As the rate of elderly population and lifetime expectancy increase in time, the prevalence of late onset AS and SpA will increase. Age may be a modifier for the clinical findings and radiological features of this group of diseases. Clinical findings like PMR or pitting edema can be seen in rheumatologic diseases (including AS and SpA) in the elderly patients and can be related with the onset age of the disease rather than being a normal clinical finding of the disease [20-22].

CONCLUSION

We showed in this study that early and late onset AS patients can present with different clinical, laboratory, and genetic features. Late onset AS patients are characterized with a lower frequency of HLA-B27 positivity, lower levels of inflammatory markers, delay in diagnosis and lower usage of MTX and anti-TNF-alpha. There is no satisfactory literature about late onset AS yet. For this reason, the clinical features, survey, and treatment options of late onset AS deserve more attention in the future. There is a definite need for multicenter prospective and retrospective studies about this subject.

DECLARATION OF INTERESTS

The authors declare no conflict of interests.

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