Clinical Features of Late-onset Ankylosing Spondylitis: Comparison with Early-onset Disease

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ABSTRACT. ***Objective.*** Ankylosing spondylitis (AS) is generally observed in young patients but can occur later in life or in persons ≥ 50 years of age. Our objective was to characterize the clinical features of late-onset AS in a large multicenter national cohort.

Methods. We studied late-onset AS in the National Registry of Spondyloarthritis of the Spanish Society of Rheumatology (REGISPONSER database) cohort (n = 1257), of whom 3.5% had onset at age ≥ 50 years versus a control group with onset at < 50 years.

Results. There were no differences between late-onset and early-onset AS according to sex and family history of spondyloarthropathies. Patients in the late-onset group more often showed involvement of the cervical spine (22.7% vs 9.7%; p = 0.03) and arthritis of the upper (13.6% vs 3.0%; p = 0.002) and lower limbs (27.3% vs 15.2%; p = 0.03) as first manifestations than did patients in the early-onset group. A higher percentage of mixed forms (axial and peripheral joint disease) during the course of the disease was also recorded in the late-onset group (50% vs 24%; p = 0.0001).

Conclusion. Our study suggests that age at onset of AS affects the patients' presenting clinical form. Arthritis of the upper limbs requires a differential diagnosis with other conditions frequent in patients over 50 years of age, such as rheumatoid arthritis or crystal-induced arthropathy. (J Rheumatol First Release March 15 2012; doi:10.3899/jrheum.111082)

Key Indexing Terms:
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The clinical expression of some inflammatory diseases, including the presenting manifestations, clinical evolution, and prognosis, may depend on the age at onset. For example, advanced age modifies the expression of systemic lupus erythematosus (SLE) with a lower incidence of serositis, interstitial pneumonia, and pancytopenia[1,2] and is recognized to have a less aggressive course than younger-onset disease[3]. On the other hand, elderly onset rheumatoid arthritis (RA) has been reported to differ from younger-onset RA by a higher frequency of systemic features and more frequent involvement of large joints[4]. Ankylosing spondylitis (AS) is the major subtype of an interrelated heterogeneous group of inflammatory rheumatic diseases now named spondyloarthritides. Clinical features of this group include spinal and peripheral joint oligoarthritis (predominantly of the lower limbs), enthesitis, and at times, specific organ involvement such as anterior uveitis, psoriasis, and chronic inflammatory bowel disease (IBD)[5,6]. Five subgroups are differentiated clinically: AS, reactive arthritis, psoriatic arthritis (PsA), IBD-associated arthritis (or enteropathic arthritis), and undifferentiated forms. These disorders show familial aggregation, are typically associated with genes of the major histocompatibility complex, particularly HLA-B27, and usually begin in young or middle-aged adults[6,7].

Clinical onset of AS after the age of 50 years is uncommon. Late-onset AS is characterized by severe disease, marked elevation of laboratory measurements of inflammation, and more frequent involvement of the peripheral joints (predominantly the shoulders) and the cervical spine as compared with early-onset AS[8,9]. Some patients with late-onset AS present with a clinical spectrum very similar to that found in polymyalgia rheumatica[10], sarcoidosis[11], or reflex sympathetic dystrophy syndrome[12]. As the population ages and the life expectancy of individuals increases, the

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prevalence of late-onset AS will rise. In addition, AS may also be misdiagnosed in some patients whose disease has not been recognized at a young age despite spinal symptoms for many years. For these reasons and given the paucity of data in the literature, the clinical spectrum and outcome of late-onset AS deserve further attention[13]. Moreover, in clinical series of late-onset AS previously reported[8,14,15], patients with a history of IBD or psoriasis were not excluded.

Our study aimed to characterize the clinical features of late-onset AS in comparison with early-onset patients in a national multicenter cohort included in a large Spanish database of patients with AS.

MATERIALS AND METHODS

In April 2004, the Spanish Spondyloarthropathy Study Group of the Spanish Society of Rheumatology began the National Registry of Spondyloarthritis [Registro Español de Espondiloartritis de la Sociedad Española de Reumatología (REGISPONSER)]. The registry is available through a computerized Internet database accessible to all participating members (website: http://biobadaser.ser.es/cgi-bin/regisponser/index.html). Methodological and organizational details of the project have been described[16,17]. Twelve rheumatology departments from 8 different cities were selected from those that have agreed to participate in the registry on the basis of the best availability to treat patients with spondyloarthritis (SpA). These centers represent a broad sociodemographic spectrum of the population treated by the Spanish health system. All centers can be considered as a reference for rheumatic diseases in their area. All participating rheumatologists were required to include all patients registered consecutively who fulfilled the inclusion criteria, up to a minimum of 100 patients per center[17].

Briefly, the inclusion criteria for the registry were fulfillment of the classification criteria from the European Spondylarthropathy Study Group[18], blood tests available within 15 days of the inclusion visit, a complete radiographic study within the previous year, and agreement to complete all self-administered questionnaires. The inclusion period was set at 12 months. All patients gave their consent to participate. The Ethics Committee of the University Hospital Reina Sofia approved the study.

For each patient, the following data were registered: age, sex, employment-related variables and habits; time (year) of diagnosis; signs and symptoms (inflammatory back pain, peripheral arthritis, extraaxial/extraskeletal effects) at diagnosis; specific rheumatic disorder (AS, PsA, reactive arthritis, IBD-associated arthritis, undifferentiated arthritis); clinical form at onset (peripheral, enthesitic, extraarticular, or mixed); and family history of inflammatory rheumatic disease. Inflammatory back pain was defined as low back pain and stiffness for > 3 months that improves with exercise but is not relieved by rest. Peripheral arthritis usually affected the large joints of the arms and legs, including the elbows, wrists, knees, and ankles. Enthesitis was defined as inflammation of the sites where tendons or ligaments insert into the bone. The extraarticular disease manifestations were recorded by physical examination. For the evaluation of disease status, the following anthropometric measures were used: occipit-to-wall distance, modified Schober's test, lateral flexion of lumbar spine, thoracic expansion, cervical rotation, and finger-to-floor distance. As measures of disease status, we also included night pain by a 0–10 visual analog scale (VAS); physician and patient's global assessment of disease activity, also by a 0–10 VAS; and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[19] and functional capacity scored by the BAS Functional Index (BASFI)[20]. Damage was indicated by the radiological assessment valued by the BAS Radiology Index (BASRI)[21], both for spine and total (BASRI spine + BASRI hips). The existence of erosions, osteophytes, and protrusions in hips was also assessed. Laboratory tests included the erythrocyte sedimentation rate (ESR), C-reactive protein, and HLA-B27 status. Current treatment and quality of life were also recorded.

For our study, we selected 1257 patients diagnosed with AS according to the modified New York criteria[22]. Patients with IBD or psoriasis were excluded. Age ≥ 50 years at the onset of symptoms was considered the cut-off age for late-onset AS. Patients were grouped into late-onset and early-onset AS. The definition of the onset of disease corresponded to the day of appearance of the first manifestation of AS. In both groups, the following data were compared: (1) epidemiological variables (duration of disease and diagnostic delay); (2) family history of AS, HLA-B27, and sex; (3) clinical manifestations, including signs and symptoms at diagnosis, clinical form at onset of disease (axial, peripheral, mixed), involvement of the cervical spine, shoulder and hip, extraarticular manifestations [uveitis, dactylitis (inflammation of either a finger or a toe), prostatitis, cardiac involvement (of the aorta and related structures, conduction abnormalities, left ventricular dysfunction), as well as renal, neurological and pulmonary involvement]; (4) physical examination-related variables (thoracic expansion, Schober's test, finger-to-floor distance, occipit-to-wall distance, and lateral flexion); (5) disease activity-related variables including ESR, serum C-reactive protein (CRP), and BASDAI; (6) the functional index BASFI; and (7) radiographic data (BASRI total and BASRI spine).

Statistical analysis. Categorical variables were compared with the chi-square test and continuous variables with Student's t test for independent samples. Simple linear regression analysis was used to assess the relationship of age at onset (< 50 yrs and ≥ 50 yrs) with disease activity (ESR and PCR) and radiographic data (BASRI total). Statistical significance was set at $p < 0.05$.

RESULTS

Late-onset AS was diagnosed in only 44 patients (3.5%). The mean (SD) age of patients was 64 (7.1) years in the late-onset group and 47 (12.7) years in the early-onset group. In both groups, the distribution by sex was similar, with a predominance of men (75%) as well as history of AS in first-degree relatives (13.6% vs 14.6%) or percentage of patients positive for HLA-B27 (82.4% vs 72.2%). Patients in the early-onset group compared with the late-onset group showed a longer duration of disease [22.2 (13.1) vs 8.8 (7.1) yrs; $p < 0.001$] and delay in establishing the diagnosis [8.2 (9.5) vs 2.9 (4.0) yrs; $p = 0.0001$]. The percentage of patients treated with anti-tumor necrosis factor-α agents was similar (late-onset group 15.8%, early-onset group 19.1%).

In relation to clinical manifestations at diagnosis (Table 1), neck pain (cervical spine) and peripheral arthritis of the lower and upper limbs were significantly more frequent among patients in the late-onset group. On the other hand, a higher percentage of mixed forms (axial and peripheral joint disease) and a lower percentage of axial forms during the course of the disease were also recorded in the late-onset group (Table 1). Involvement of the cervical spine also occurred in a significantly higher percentage of patients in the late-onset group. Uveitis was significantly less frequent in the late-onset group, whereas cardiac involvement was significantly more frequent among patients with late-onset AS in comparison with early-onset patients; the distribution of other extraarticular manifestations was similar (Table 1).

There were no statistically significant differences between late-onset and early-onset groups in physical examination-related variables, measures of disease activity, and radiographic data (Table 2).

Table 1. Clinical-related variables in patients with late-onset (age ≥ 50 yrs) and early-onsert (age < 50 years) ankylosing spondylitis. Data expressed as no. (%).

Variables	Early-onset, n = 1213	Late-onset, n = 44	p
Clinical manifestations at onset			
Back pain	870 (71.7)	26 (59.1)	0.120
Sacroiliac joint pain	510 (42.0)	16 (36.4)	0.470
Neck pain (cervical spine)	118 (9.7)	10 (22.7)	0.03
Hip pain	45 (3.7)	2 (4.5)	0.770
Arthritis, lower limbs	185 (15.2)	12 (27.3)	0.03
Arthritis, upper limbs	36 (3.0)	6 (13.6)	0.002
Enthesitis	88 (7.2)	4 (9.1)	0.640
Dactylitis	10 (0.8)	1 (2.3)	0.320
Clinical form during disease course			
Axial	907 (74.8)	21 (47.7)	0.004
Mixed	300 (24.7)	23 (52.3)	0.0001
Cervical spine involvement	118 (9.7)	10 (22.7)	0.005
Shoulder involvement	166 (13.7)	10 (22.7)	0.095
Hip involvement	267 (22.0)	8 (18.2)	0.519
Exraarticular manifestations			
Uveitis	283 (23.3)	2 (4.5)	0.003
Dactylitis	43 (3.5)	3 (6.8)	0.259
Prostatitis	9 (0.7)	0	0.261
Neurological	10 (0.8)	1 (2.3)	0.225
Renal	24 (2.0)	2 (4.5)	0.280
Pulmonary	19 (1.6)	1 (2.3)	0.320
Cardiac	23 (1.9)	3 (6.8)	0.03

Table 2. Differences between patients with late-onset (age ≥ 50 yrs) and early-onset (age < 50 yrs) ankylosing spondylitis regarding physical examination-related variables, disease activity, and radiographic data. Data expressed as mean (SD).

Variables	Early-onset, n = 1213	Late-onset, n = 44	p
Physical examination			
Thoracic expansion, cm	3.79 (2.21)	3.47 (2.08)	0.35
Schober's test	2.93 (1.78)	2.83 (1.38)	0.66
Finger-to-floor distance, cm	14.21 (18.73)	19.18 (15.36)	0.83
Occiput-to-wall distance, cm	4.49 (6.04)	4.69 (6.57)	0.82
Lateral flexion, cm	22.13 (19.64)	27.67 (21.71)	0.07
Disease activity			
ESR, mm	18.0 (16.29)	23.07 (17.62)	0.051
Serum PCR, mg/dl	8.83 (12.75)	12.10 (25.91)	0.557
BASDAI	4.16 (2.35)	3.95 (2.35)	0.557
BASFI	3.86 (2.71)	3.68 (2.79)	0.67
Radiographic data			
BASRI total (spine + hip)	7.07 (4.10)	7.75 (4.16)	0.27
BASRI spine	6.24 (3.40)	6.82 (3.41)	0.28

ESR: erythrocyte sedimentation rate; PCR: polymerase chain reaction; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: BAS Functional Index; BASRI: BAS Radiology Index.

In the early-onset group, a significant correlation between duration of disease and BASRI total was observed [coefficient of determination (R^2) = 0.512, p < 0.0001], whereas in the late-onset group, no significant correlation was found (R^2 = 0.30, p = 0.051).

DISCUSSION

It is well documented that immunocompetence declines with age. Age-related changes in the immune system are expressed by inflammatory conditions that usually develop in the elderly (e.g., polymyalgia rheumatica) or distinct clinical features when SLE or RA begins later in life. AS is classically a disease that occurs early in life, usually in the second and third decade, and clinical onset after the age of 50 is uncommon[23]. Moreover, the concept and definition of disease duration in patients with AS is ambiguous, and often many years pass between the onset of symptoms and diagnosis[24]. The first published studies of patients with late-onset spondylitis reported peculiar peripheral forms similar to those found in patients with remitting seronegative symmetrical synovitis with pitting edema[15] or reflex sympathetic dystrophy syndrome[12], frequently associated with the HLA-B27 class I antigen and minimal involvement of the axial skeleton.

Apart from these initial descriptions of late-onset AS, a few comparative studies related to age at onset of disease have been carried out. These studies, however, include small series of patients and are very heterogeneous because different subtypes of inflammatory rheumatic diseases are grouped and different cutoffs were defined as the age for late onset. Calin, *et al*[9] compared some clinical variables (uveitis, family history, hip pain, shoulder pain, and cervical mobility) between 76 patients with AS with age at onset from 35 to 45 years and 76 matched controls whose age at onset was 20–25 years. Only patients with late onset experienced significantly higher shoulder pain than controls. In the study by Caplanne, *et al*[8], 8 patients in whom the first episode of inflammatory AS was recorded after 55 years of age were compared with 32 patients with early-onset AS. Patients with IBD were not excluded, and were significantly more frequent in the late-onset group (37.5% vs 6.3%; p = 0.02). Patients with psoriasis were also included. It was found that patients with late-onset disease had significantly more cervical and dorsal pain, anterior chest wall involvement, and raised ESR. Olivieri, *et al*[25] studied a group of 23 patients with undifferentiated SpA after the age of 45, and the presenting form in these patients was similar to that reported by Dubost and Sauvezie[15], that is, peripheral arthritis with pitting edema on the dorsum of feet. Predominant peripheral involvement has also been reported in patients with late-onset PsA[26]. In the study by Punzi, *et al*[27], radiographic progression 2 years after diagnosis was more evident in the elderly-onset group (> 60 years) than in patients with younger-onset PsA. However, despite the heterogeneity of these studies, patients with inflammatory rheumatic disorders and clinical onset after the age of 50 years present a higher proportion of peripheral forms.

Our study has several differences from previous publications, including a retrospective cohort design, the use of 50 years of age to define late-onset AS, and the exclusion of patients with IBD or psoriasis. Data from patients were collected from a prospective nationwide registry following predefined diagnostic criteria and standardized clinical and radiological measures of disease activity. On the other hand, our series of 44 patients with late-onset spondylitis and 1213 patients with early-onset disease represent the largest comparison to date aiming to assess the influence of age on disease expression of AS. The late-onset group was characterized by a higher occurrence of peripheral arthritis in both the upper and lower extremities as compared with early-onset patients, although the percentage of patients with isolated sacroiliac joint involvement and shoulder involvement was similar in both groups. During the course of the disease, a significantly higher percentage of mixed forms (axial and peripheral) was found in patients older than 50 years. Shoulder involvement and hip involvement was similar in late-onset and early-onset AS patients. Involvement of the cervical spine was frequent in the older group both at the onset of the disease and during the course of illness.

In agreement with previous studies[8,9], there were no differences between late-onset and early-onset patients in relation to the genetic expression (family history of AS in first-degree relatives and HLA-B27 positivity). Regarding the extraarticular manifestations, acute anterior uveitis was more frequent in the early-onset group. Cardiac involvement was more common among patients with late-onset disease but the higher incidence of cardiovascular disorders in elderly patients (e.g., hypertension) may account for this finding. On the other hand, the similar distribution of peripheral arthritis in the 2 study groups may justify the lack of differences in acute-phase reactants (ESR and PCR). Other measures of disease activity, such as BASDAI and BASFI, were also similar. In relation to progression of AS, although duration of the disease was higher in the early-onset group, differences in physical examination-related variables were not found. Moreover, studies[28] have shown that progression of radiographic findings is a function of disease duration, but in our study, differences were not documented in BASRI total and BASRI spine between patients with early-onset and those with late-onset AS. However, in the early-onset group, duration of disease was correlated with BASRI total.

Our study provides further evidence for the existence of different clinical patterns between late-onset and early-onset subsets of patients with AS, and evidence that mixed forms (axial and peripheral) are more frequent in the clinical expression of AS after 50 years of age.

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REFERENCES

1. Baker SB, Rovira JR, Campion EW, Mills JA. Late onset systemic lupus erythematosus. Am J Med 1979;66:727-32.
2. Maddison PJ. Systemic lupus erythematosus in the elderly. J Rheumatol Suppl. 1987 Jun;14:182-7.
3. Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P, et al. Systemic lupus erythematosus: Clinical and immunologic patterns of disease expression in a cohort of 1,000 patients. Medicine 1993;72:113-24.
4. Bajocchi G, La Corte R, Locaputo A, Govoni M, Trotta F. Elderly onset rheumatoid arthritis: Clinical aspects. Clin Exp Rheumatol 2000;4 Suppl 20:S49-50.
5. FitzGerald O, Maksymowych WP. What are the spondyloarthropathies? Best Pract Res Clin Rheumatol 2010;24:575-7.
6. Toussirot E, Wendling D. Late-onset ankylosing spondylitis and related spondylarthropathies: Clinical and radiological characteristics and pharmacological treatment options. Drugs Aging 2005;22:451-69.
7. Kataria RK, Brent LH. Spondyloarthropathies. Am Fam Physician 2004;15:2853-60.
8. Caplanne D, Tubach F, Le Parc JM. Late onset spondyloarthropathy: Clinical and biological comparison with early onset patients. Ann Rheum Dis 1997;56:176-9.
9. Calin A, Elswood J, Edmunds L. Late onset ankylosing spondylitis — A distinct disorder? Br J Rheumatol 1991;30:69-70.
10. Olivieri I, Garcia-Porrua C, Padula A, Cantini F, Salvarani C, Gonzalez-Gay MA. Late onset undifferentiated spondyloarthritis presenting with polymyalgia rheumatica features: description of seven cases. Rheumatol Int 2007;27:927-33.
11. Sezer I, Melikoglu MA, Cay HF, Kocabas H, Kacar C. A co-occurrence of sarcoidosis and ankylosing spondylitis: A case report. Rheumatol Int 2008;28:605-7.
12. Dubost JJ, Soubrier M, Ristori JM, Guillemot C, Bussière JL, Sauvezie B. Late-onset spondyloarthropathy mimicking reflex sympathetic dystrophy syndrome. J Bone Spine 2003;70:226-9.
13. Toussirot E. Late-onset ankylosing spondylitis and spondylarthritis. An update on clinical manifestations, differential diagnosis and pharmacological therapies. Drugs Aging 2010;27:523-31.
14. Cohen MD, Ginsburg WW. Late-onset peripheral joint disease in ankylosing spondylitis. Ann Rheum Dis 1982;41:574-8.
15. Dubost JJ, Sauvezie B. Late onset peripheral spondyloarthropathy. J Rheumatol 1989;16:1214-7.
16. Ariza R and Grupo de Estudio de Espondiloartropatías de la SER (GRESSER). REGISPONSER. Reumatol Clin 2005;Suppl 1:S7-11.
17. Collantes E, Zarco P, Muñoz E, Juanola X, Mulero J, Fernández-Suiero JL, et al. Disease pattern of spondyloarthropathies in Spain: Description of the first national registry (REGISPONSER) — extended report. Rheumatology 2007;46:1309-15.
18. Dougados M, van der Linden S, Juhlin R, Huitfeldt B, Amor B, Calin A, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum 1991;34:1218-27.
19. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: The Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286-91.
20. Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, et al. A new approach to defining functional ability in ankylosing spondylitis: The development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 1994;21:2281-5.
21. Mackay K, Mack C, Brophy S, Calin A. The Bath Ankylosing Spondylitis Radiology Index (BASRI). A new validated approach to diseases assessment. Arthritis Rheum 1998;41:2263-70.

22. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361-8.
23. Feldtkeller E, Bruckel J, Khan MA. Scientific contributions of ankylosing spondylitis patient advocacy groups. Curr Opin Rheumatol 2000;12:239-47.
24. Davis JC, Dougados M, Braun J, Sieper J, van der Heijde D, van der Linden S. Definition of disease duration in ankylosing spondylitis: Reassessing the concept. Ann Rheum Dis 2006;65:1518-20.
25. Olivieri I, Padula A, Pierro A, Favaro L, Oranges GS, Ferri S. Late onset undifferentiated seronegative spondyloarthropathy. J Rheumatol 1995;22:899-903.
26. López-Montilla MD, González J, Martínez FG, Fernández-Moreno JR, Collantes E. Clinical features of late onset psoriatic arthritis. Exp Gerontol 2002;37:441-3.
27. Punzi L, Pianon M, Rossini P, Schiavon F, Gambari PF. Clinical and laboratory manifestations of elderly onset psoriatic arthritis: A comparison with younger onset disease. Ann Rheum Dis 1999;58:226-9.
28. Brophy S, Mackay K, Al-Saidi A, Taylor G, Calin A. The natural history of ankylosing spondylitis as defined by radiological progression. J Rheumatol 2002;29:1236-43.