Occurrence of fibromyalgia in patients with ankylosing spondylitis

Valderilio Feijó Azevedo[1], Eduardo dos Santos Paiva[1], Lúcio Ricardo Hiurko Felippe[2], Ranieri Amorim Moreira[3]

ABSTRACT

Introduction: Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects the axial skeletal system, causing pain and functional incapacity. To measure the impact of AS on patient's life, questionnaires are used to assess disease activity (BASDAI); functional incapacity (BASFI); and quality of life (ASQoL). Fibromyalgia (FM) is one of the most common causes of generalized pain and can coexist with other diseases; it can be assessed by the Fibromyalgia Impact Questionnaire (FIQ). Few studies have demonstrated correlations between FM and AS. The present study obtained data regarding the epidemiologic profile of patients with AS and FM and evaluated the prevalence of FM in patients with AS. The FM influence on BASDAI, BASFI and ASQoL test scores was assessed. **Patients and Method:** A total of 71 patients with AS, diagnosed according to the modified New York criteria, were studied. Clinical and functional assessment was performed and BASDAI, BASFI and ASQoL tests were applied. Patients with a diagnosis of FM were evaluated through the FIQ. **Results:** Eleven patients met the criteria for FM; thus a FM prevalence of 15% was observed among the patients with AS. FM was more prevalent among women (3.8:1). Age at disease onset (AS) was 27.5 years. The HLA-B27 antigen was positive in most of them (80.4%). When comparing BASDAI, BASFI and ASQoL test means, it was observed that values are significantly higher ($P < 0.01$) among patients with FM. We concluded that the coexistence of FM can worsen AS activity aspects, as well as functional incapacity and quality of life.

Keywords: ankylosing spondylitis, fibromyalgia, health impact profile evaluation.

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects mainly the spine and can result in stiffness and progressive axial skeletal system functional limitation.[1,2] The disease is more frequent in young adults, with age at onset generally ranging from 20 to 40 years and is more prevalent in the male sex (3:1), Caucasians and HLA-B27-positive individuals.[2,3] It is part of the spondyloarthritis complex, which is strongly correlated with HLA-B27, whose presence varies from 80% to 98% of the cases.[4]

The initial clinical presentation is low back pain with an inflammatory-rhythm associated with morning stiffness.[1,2] In the spine, AS causes ligament ossifications, vertebral fusion, osteoporosis, resulting in a remodeled and weakened vertebral column, with a strong tendency toward fractures and deformation.[1,5] The enthesopathies are characterized by inflammation at the tendon and/or ligament insertions on bones and affect mainly the calcaneal tendon insertion and plantar fascia.[1]

The modified New York criteria, which combine clinical and radiographic features, are most commonly used to confirm

Received on 04/22/2010. Approved on 11/11/2010. We declare no conflict of interest.
Hospital de Clínicas da Universidade Federal do Paraná – HC UFPR, Brazil.
1. Assistant Professor of Rheumatology, MD
2. Psychologist; Undergraduate Medical Student at UFPR.
3. Undergraduate Medical Student at UFPR
Correspondence to: Valderilio Feijó Azevedo. Rua Lamenha Lins 1110, ap 11ª, Rebouças. Curitiba, PR, Brazil. CEP: 80250-020. E-mail: valderilio@hotmail.com.

AS diagnosis. The presence of a clinical criterion, as well as of a radiographic criterion, is necessary to attain AS diagnosis.[6]

In the last decades, several evaluation tools have been proposed due to the appearance of more effective medications for the treatment of AS, as well as the need to attain a more objective and standardized patient's clinical assessment.

In 1994, Garret *et al.* presented a questionnaire aimed at evaluating AS activity[7]. The BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) test is a six-question questionnaire comprising domains related to fatigue, spinal pain, pain and articular symptoms, pain related to enthesis involvement and two questions related to the quality and amount of morning stiffness.

The score is measured using visual analog scales (VAS) from 0 to 10 (0 = good; 10 = poor). It is currently considered one of the most important tools for use in clinical assays.[8]

In 1994, Calin *et al.* published the BASFI (Bath Ankylosing Spondylitis Functional Index), a questionnaire that aims at assessing functional limitation in patients with AS.[9] The test includes eight items related to activities of daily living and two items that measure patient skill when dealing with everyday routine.[9]

Both BASFI and BASDAI criteria have been well accepted due to their functionality, reproducibility, and sensitivity when assessing AS characteristics and its evolution. Many countries have already carried out the validation of this method[10,11] according to their own language, as Brazil has done.

Due to the importance of quality of life assessment as an end-point measurement in clinical studies, questionnaires such as the ASQoL (Ankylosing Spondylitis Quality of Life Questionnaire) have been increasingly used. The test comprises 18 questions with yes or no answers, which result in a score from 0 to 18, with the highest score being associated with a worse quality of life (QoL). It is the only tool originally developed as a specific QoL measure in AS.[8,12]

Fibromyalgia (FM) is one of the most common causes of generalized musculoskeletal pain. Its etiology is yet to be elucidated, but it is believed to be an inflammatory process. It is considered to be a pain amplification syndrome, associated with a central nervous system sensitization mechanism.[13,14] It is more frequent in females and most patients are between 35 and 50 years of age. The physical examination typically discloses the absence of synovitis and/or other symptoms indicating inflammatory disease; the main characteristic is the presence of tender points identified on palpation.[14,15]

FM can coexist with other rheumatologic diseases, such as psoriatic arthritis (24%),[16] rheumatoid arthritis (25%),[13] systemic lupus erythematosus (30%)[13] and Crohn's disease (49%).[17] The diagnosis is essentially a clinical one and is based on the identification of tender points and the absence of symptoms or laboratory findings that can indicate an inflammatory or degenerative disease. In this sense, the inflammatory activity tests, muscle enzymes and electromyography results are normal.[13,15] The American College of Rheumatology (ACR) criteria are used in research: 1) chronic generalized pain in both sides of the body, both axial and peripheral, below and above the waist; 2) presence of 11 of 18 tender points.[18]

There have been few studies that demonstrated a correlation between FM and AS. A single article has been recently published, which showed FM prevalence in patients with AS. This same article also pointed out the influence of FM coexistence on the patient assessment test scores.[19]

The present study aimed at obtaining data regarding the epidemiologic profile of patients with AS and FM and identifying FM prevalence in patients with AS. It also aimed at comparing the functional indices and assessing whether the coexistence of the FM picture can interfere with the disease activity evaluation (BASDAI), functional assessment (BASFI) and AS patient quality of life (ASQLo) test scores.

PATIENTS AND METHOD

Target population

The study evaluated 71 patients with AS diagnosed according to the modified New York criteria, treated at the Rheumatology Outpatient Clinic of Hospital de Clínicas de Curitiba, from April to December 2009. Patients that presented another concomitant rheumatologic disease that could justify the presence of chronic generalized pain were excluded from the study. All patients gave their free and informed consent to participate in the study, which was approved by the Ethics Committee in Research of the do Hospital, protocol #1890.057/2009-03.

Procedures

A cross-sectional, observational epidemiologic study of prevalent cases was carried out. The patients answered a questionnaire that included the following information: birth date, age, sex, ethnicity, symptom onset date and family history concerning the presence of AS in first-degree relatives such as siblings or parents. Data from the medical files were collected regarding the HLA-B27 antigen screening. Disease activity assessment was carried out by applying the BASDAI questionnaire; functional assessment by applying the BASFI questionnaire and patient quality of life was evaluated through the ASQoL. Subsequently,

the patients were assessed regarding the presence of FM according to the criteria established by the ACR and cases were considered positive in the presence of the two concomitant criteria.

Data processing and analysis

The patients were divided in two groups: with and without FM. The BASDAI, BASFI and ASQoL test scores of both groups were compared by Student's t test and Wilcoxon's test.

RESULTS

The epidemiologic data of the 71 patients is shown in Table 1. Of these, 84.5% were males and 15.5% were females (a male:female ratio of 5.5:1). Of the 71 assessed patients, 11 (15%) met the ACR critreria for FM, of whom 5 (45.5%) were males and 6 (54.5%) were females. FM prevalence was 15% among the AS patients, with a female:male ratio of 3.8:1.

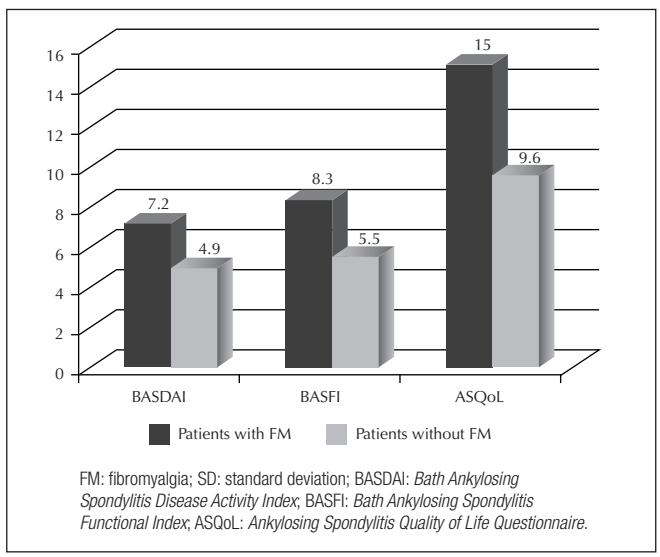
Patients' mean age was 43.67 (standard deviation [SD] = 11.78), ranging from 19 to 69.3 years. Mean age at symptom onset was 27.5 years (SD = 11.80). Mean symptom duration was 16.59 years (SD = 9.64). Most patients were Caucasians (70.4%) or Brazilian mulattos (21.1%). Only 13.2% of the patients had a positive family history for spondyloarthritis. Of the 71 assessed patients, 46 (65%) had information on the HLA-B27 antigen screening in their medical files, which was positive in the majority of them (80.4%).

The comparative data of the two subgroups are shown in Table 2 and Figure 1.

Table 1
Epidemiologic and clinical data of 71 study participants with ankylosing spondilytis diagnosis

Characteristics	Values
Total patients	71
Men	54 (84.5%)
Women	17 (15.5%)
Patients with Fibromyalgia	11 (15%)
Men	5 (45.5%)
Women	6 (54.5%)
Age (years)	43.67 (SD = 11.78)
Age at symptom onset (years)	27.5(SD = 11.80)
Symptom duration (years)	16.59 (SD = 9.64)
Family History	
Positive (%)	13.2
Negative (%)	86.8
HLA-B27	
Positive (%)	80.4
Negative (%)	16.6

SD: standard deviation.



FM: fibromyalgia; SD: standard deviation; BASDAI: *Bath Ankylosing Spondylitis Disease Activity Index*; BASFI: *Bath Ankylosing Spondylitis Functional Index*; ASQoL: *Ankylosing Spondylitis Quality of Life Questionnaire.*

Figura 1.
Comparison between the BASDAI, BASFI and ASQoL test score means in the 2 subgroups with and without FM. All tests showed statistical significance, confirmed by Student's t test and Wilcoxon's test.

Table 2
BASDAI, BASFI and ASQoL test comparative data in patients with and without FM

Testes	Patients with FM n = 11	Patients without FM n = 60	P-value (Student's t test)	P-value (Wilcoxon's test)
Number of Patients	11	60		
BASDAI	7.2 (SD = 1.61)	4.9(SD = 2.38)	< 0.001	= 0.002940
BASFI	8.3 (SD = 1 .03)	5.5 (SD = 3.11)	< 0.001	= 0.001992
ASQoL	15(SD = 2.00)	9.6(SD = 5.55)	= 0.0019	= 0.001884

FM: fibromyalgia; SD: standard deviation; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index;
BASFI: Bath Ankylosing Spondylitis Functional Index; ASQoL: Ankylosing Spondylitis Quality of Life Questionnaire.

DISCUSSION

Epidemiological data of the present study corroborate the data found in the literature. Mean age at disease onset in our patients was 27.5 years, which is within the 20-40 range, that is, symptom onset typically at the young adult age range.[4] Prevalence was higher in the male sex (5.5:1) and a little higher when compared to literature data (3:1).[4] The disease showed to be more prevalent in Caucasians (70.4% of the assessed patients). The HLA-B27 antigen was positive in most of them (80.4%).[20]

Although a low incidence of positive family history for spondyloarthritis was observed in most patients (86.8%), the genetic factors classically contribute to a higher susceptibility to disease development. It was observed that the risk of developing AS is much higher (10 to 20-fold higher) among relatives of patients with positive HLA-B27, when compared to the general population with positive HLA-B27.[21]

A single study identified the FM prevalence among patients with AS.[19] Aloush *et al.* studied a group of 36 patients with an AS diagnosis, of which 18 were males and 18 females. The authors confirmed the FM diagnosis in 50% of the females, but did not confirm it in any of the men. The investigators observed that patients that presented the two diseases concomitantly had more severe functional impairment, which resulted in higher scores at the BASDAI and BASFI tests, when compared to the scores of patients with only one disease. An important bias was present and raised questions regarding whether the presence of FM could influence the result of the functional assessment tests: the diagnosis of FM was established in the group of female patients only.[19] It is known that AS manifestation is different between genders, having a worse prognosis among men.[22]

In our study, 71 patients were assessed and FM prevalence was 15%; in this group of patients, 45.5% were males and 54.5% were females. We evaluated a more balanced sample between men (45.5%) and women (54.5%) among those individuals with FM. We confirmed significantly higher scores at the BASDAI ($P < 0.001$ at Student's *t* test and $P = 0.002940$ at Wilcoxon's test) and BASFI ($P < 0.001$ at Student's *t* test and $P = 0.001992$ at Wilcoxon's test) tests. Additionally, we compared the ASQoL test results and also observed higher scores ($P = 0.0019$ at Student's *t* test and $P = 0.001884$ at Wilcoxon's test) among the patients with FM. Heikkilä *et al.,*[23] stressed the correlations found between the two diseases, in spite of the predominance of each one of them at different ages and in different sexes. When assessed by laboratory tests, only AS presents characteristics of an inflammatory disease. However, from a clinical perspective, both lead to a decrease in functional and work capacity in a very similar way.[23-25] It is noteworthy the fact that AS and FM share many symptoms. The diagnosis of AS is based on the presence of chronic vertebral pain associated with morning stiffness, which are, in turn, frequent complaints in FM[18]. Anxiety, depression, fatigue, and sleep disorder complaints are significant in FM and also very often reported by patients with AS. These problems are strongly associated with the pain.[26-28]

Currently, the indication for the use of biologicals in AS is based on the activity index, among others.[22] Based on our results, we suggest that before biologicals are prescribed, patients with AS should be assessed regarding the possibility of concomitant FM and those showing positive criteria should be adequately treated and reassessed.

One limitation of the present study is the lack of a control population. However, even though the study design does not include a control group, it is the largest series on FM among patients with AS published to date. A 15% prevalence of FM was verified among patients with AS, with the concomitance being evenly distributed between genders. Additionally, the data showed that the concomitant presence of FM can aggravate the symptoms of disease activity, functional impact, and compromise the quality of life of patients with AS.

REFERÊNCIAS

REFERENCES

1. Sampaio-Barros P, Azevedo VF, Bonfiglioli R, Campos WR, Carneiro SCS, Carvalho MAP *et al*. Consenso Brasileiro de Espondiloartropatias: espondilite anquilosante e artrite psoriásica diagnóstico e tratamento - Primeira revisão. Rev Bras Reumatol 2007; 47(4):233-42.
2. Dougados M. Diagnostic features of ankylosing spondylitis. Br J Rheumatol 1995; 34:301-5.
3. Van Der Linden S, Van Der Heijde D. Ankylosing spondylitis: clinical features. Rheum Dis Clin North Am 1998; 24(4):663-76.
4. Reveille JD, Ball EJ, Khan MA. HLA-B27 and genetic predisposing factors in spondyloarthropathies. Curr Opin Rheumatol 2001; 13(4):265-72.
5. Rudwaleit M, Metter A. Inflammatory back pain in ankylosing spondylitis: a reassessment of the clinical history for application as classification and diagnostic criteria. Arthritis Rheum 2006; 54(9):569-78.
6. 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(4):361-8.
7. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankyosing Spondylitis Disease Activity Index. J Rheumatol 1994; 21(12):286-91.
8. Torres T, Ciconelli R. Instrumentos de Avaliação em Espondilite Anquilosante. Rev Bras Reumatol 2003; 46(1):52-9.

9. 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(12):2281-5.
10. Heikkilä S, Viitanen JV, Kautianen H, Kauppi M. Evaluation of the finnish versions of the functional indices BASFI and DFI in spondylarthropathy. Clin Rheumatol 2000; 19(6):464-9.
11. Udrea G, Ciobanu C, Mihai C, Stoica V, Suteanu S, Van Der Heijde D *et al*. Evaluation of Romanian version of the Bath Ankylosing Spondylitis functional index (BASFI) in patients with spondylarthropathies. Romanian Journal of Internal Medicine 2004; 42(11):199-209.
12. Doward L, Spoorenberg A, Cook S, Whalley D, Helliwell P, Kay L *et al*. Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. Ann Rheum Dis 2003; 62(1):20-6.
13. Projeto Diretrizes - Sociedade Brasileira de Reumatologia. Fibromialgia. Acesso em: 20 de abril de 2010.
14. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL *et al*. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33(2):160-72.
15. Skare T. Reumatologia: princípios e prática. 2 Ed. Rio de Janeiro: Guanabara Koogan, 2007, pp. 335.
16. Buskila D, Langevitz P, Gladman DD, Urowitz S, Smythe HA. Patients with rheumatoid arthritis are tenderer than those with psoriatic arthritis. J Rheumatol 1992; 19(7):1115-19.
17. Buskila D, Odes LR, Neumann L, Odes HS. Fibromyalgia in Inflammatory bowel disease. J Rheumatol 1999; 26(5):1167-71.
18. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL *et al*. The American College of Rheumatology 1990, Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33(2):160-72.
19. Aloush V, Ablin J, Reitblat T, Caspi D, Elkayam O. Fibromyalgia in women with ankylosing spondylitis. Rheumatol Intern 2007; 27(9):865-8.
20. Brewerton DA, Caffrey M, Hart FD, James DCO, Nicholls A, Sturrock RD. Ankylosing spondylitis and HLA-B27. Lancet 1973; 1:904-7.
21. Van Der Linden SM, Valkenburg HA, De Jongh BM, Cats A. The risk of developing ankylosing spondylitis in HLA-B27 positive individuals: a comparison of relatives of spondylitis patients with the general population. Arthritis Rheum 1984; 27(3):241-9.
22. Sieper J, Braun J, Rudwaleit M, Boonen A, Zink A. Ankylosing spondylitis: an overview. Ann Rheum Dis 2002; 61(3)27:241-9.
23. Heikkilä S, Ronni S, Kautiainen HJ, Kauppi MJ. Functional impairment in spondyloarthropathy and fibromyalgia. J Rheumatol 2001; 29(7):1415-19.
24. Turan Y, Duruöz MT, Bal S, Guvenc A, Cerrahoglu L, Gurgan A. Assessment of fatigue in patients with ankylosing spondylitis. Rheumatol Intern 2007; 27(9):847-52.
25. Boonen A, Van Den Heuvel R, Van Tubergen A, Goossens M, Severens J, Van Der Heijde D *et al*. Large differences in cost of illness and wellbeing between patients with fibromyalgia, chronic low back pain, or ankylosing spondylitis. Ann Rheum Dis 2005; 64(3):396-402.
26. Dernis-Labous E, Messow M, Dougados M. Assessment of fatigue in the management of patients with ankylosing spondylitis. Rheumatology 2003; 42(12):1523-8.
27. Barlow JH, Macey SJ, Struthers GR. Gender, depression, and ankylosing spondylitis. Arthritis Care Res 1993; 6(1):45-51.
28. Hultgren S, Broman JE, Gudbjornsson B, Hetta J, Lindqvist U. Sleep disturbances in outpatients with ankylosing spondylitis questionnaire study with gender implications. Scand J Rheumatol 2000; 29(6):365-9.