A Clinical Study of Thai Patients with Spondyloarthropathy

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Abstract

Eighty-eight Thai patients (61 males and 27 females) with spondyloarthropathy (SpA) were studied. Their mean age and mean duration of the disease were 25.97 and 3.34 years respectively. In 16 cases the disease first appeared before the age of 16 or had juvenile onset. Eleven cases were ankylosing spondylitis (AS), 9 were juvenile AS (JAS), 20 were Reiter's syndrome (RS), 4 were juvenile RS, 14 were psoriatic arthritis (PsA), 27 were undifferentiated SpA (uSpA), and 3 were juvenile uSpA. Peripheral arthritis, especially oligoarthritis of the lower extremity joints, was the most common form of arthritis in all groups, except for PsA, where polyarthritis was common. Back pain and bilateral sacroiliitis were commonly seen in JAS and AS. Enthesopathy was not uncommon. Extra-articular manifestations were more common in RS patients. Acute inflammatory eye diseases were seen in 45 per cent of AS and 66 per cent of RS cases. In general, the clinical features of Thai patients with SpA were similar to those reported in other countries in Asia and the west.

Spondyloarthropathy (SpA) is a group of related disorders characterized by inflammation of the axial and/or peripheral joints, tendons, and ligaments which are attached to bone (enthesitis); absence of rheumatoid factor (RF); association with HLA-B27; and familial aggregation. The musculoskeletal symptoms are usually accompanied by extra-articular features including inflammatory eye diseases, mucocutaneous and genital lesions, and cardiac, pulmonary and bowel inflammation. It includes definite conditions such as ankylosing spondylitis (AS), Reiter's syndrome (RS) (including reactive arthritis [ReA]), psoriatic arthritis (PsA), arthritis associated with inflammatory bowel diseases (IBD), and a less well defined condition, "undifferentiated spondyloarthropathy" (uSpA).

The clinical features of SpA in western countries are well recognized and described in the

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textbook[1,2]. However, studies of the clinical features of SpA in Asia including Thailand have rarely been described. We report here our experience of the clinical features of SpA seen at a university hospital over a 6-year period and review the clinical features of SpA reported in other countries in Asia.

MATERIAL AND METHOD

The patients studied were in- and outpatients of the Division of Rheumatology, Department of Medicine, Faculty of Medicine, Chiang Mai University seen from July 1991 to September 1997. Medical histories were taken and physical examinations were performed on all patients, with special attention to the musculoskeletal and extra-articular manifestations of SpA. The diagnosis of SpA was made by using the criteria of the European Spondyloarthropathy Study Group (ESSG)[3]. The diagnosis of AS was made by using the modified New York criteria[4]. The diagnoses of RS and PsA followed the criteria used in the textbook "Spondyloarthopathies"[1]. USpA was used to describe patients who presented with asymmetric oligoarthritis of the lower extremity joints, enthesopathy, and/or inflammatory back pain that did not fulfill the criteria for the diagnosis of AS, RS, PsA, or SpA associated with IBD[5]. Cases where the disease developed before the age of 16 were classified as juvenile onset. Cases associated with human immunodeficiency virus (HIV) infection were excluded from this study.

Laboratory investigations including complete blood count, urine analysis, kidney and liver functions, and RF were performed, and appropriate radiographs of the spines and peripheral joints were taken in all patients. HLA-B27 determinations were not done, as they are not routinely available at our hospital.

RESULTS

Eighty-eight patients (61 males and 27 females) with the clinical diagnosis of SpA were identified. Sixteen patients had the disease onset before the age of 16 or had juvenile onset. Of these 16 cases, 9 had juvenile ankylosing spondylitis (JAS), 4 had juvenile RS (JRS), and 3 had juvenile uSpA (JuSpA). Among those with an adult onset there was AS in 11 cases, PsA in 14, RS in 20 and uSpA in 27. As the number of JRS and JuSpA was small, these were included in the adult group for analysis. Table 1 shows the clinical features of the patients studied. Their mean age at onset and mean duration of the disease were 25.97 and 3.34 years respectively. The mean age at onset was similar for the AS, PsA, and uSpA patients, but the duration of the disease was shorter in patients with RS and uSpA. Peripheral arthritis was the most common manifestation in all groups and was seen in 72 cases (81.81%). Spinal pain was a presentation in 16 cases (18.18%) and was more commonly seen in patients with AS. Regarding the type of peripheral arthritis at onset, asymmetric oligoarthritis was the most common type in all groups except for PsA, in which polyarthritis was common.

Table 1. Characteristics of Thai patients with spondyloarthropathy.

	Total (n=88)	JAS (n=9)	AS (n=11)	RS (n=24)	PsA (n=14)	uSpA (n=30)
Sex (M:F)	61:27	8:1	10:1	20:4	9:5	14:16
Age, in yr.	29.27±10.55	19.33±5.63	36.00±8.34	24.91±7.46	34.42±5.10	30.86±12.91
Age at onset, in yr.	25.97±10.59	12.44±2.24	28.72±8.45	23.33±6.94	29.78±7.09	29.36±12.86
Duration of disease, in yr.	3.34±4.56	6.88±4.37	7.28±6.78	1.64±2.91	4.67±5.43	1.59±2.40
Type of arthritis at onset						
Peripheral joints	72	7	6	22	12	25
Spinal pain	16	2	5	2	2	5
Type of peripheral arthritis						
Oligoarthritis	54	6	6	19	4	19
Polyarthritis	34	3	5	5	10	11

Age and duration of disease are expressed in mean ± SD

Table 2. Articular manifestations of Thai patients with spondyloarthropathy.

	Total (n=88)	JAS (n=9)	AS (n=11)	RS (n=24)	PsA (n=14)	uSpA (n=30)
Sternoclavicular	3	0	0	-	-	3
Shoulder	17	4	2	3	4	4
Elbow	19	3	0	2	6	8
Wrist	25	3	2	1	9	10
MCP	22	2	1	5	8	6
PIP	17	1	1	3	7	5
DIP	3	-	1	-	2	-
Hip	24	5	6	3	5	5
Knee	70	9	8	20	11	22
Ankle	61	6	6	17	9	23
MTP	27	1	2	7	8	9
Dactylitis	9	0	0	3	5	1
Spinal pain						
Lumbosacral	36	9	10	5	4	8
Cervical	7	2	3	-	1	1
Sacroiliitis (X-ray)						
Bilateral	27	9	11	2	3	2
Unilateral	8	0	0	4	-	4
Spondylitis (X-ray)						
Lumbosacral	15	2	9	2	-	2
Thoracic	6	1	5	-	-	-
Cervical	5	1	4	-	-	-
Tendonitis						
Achilles tendon	30	4	3	10	-	13
Plantar fascia	19	2	4	4	3	6
Other sites	7	1	0	4	-	2

MCP = metacarpophalangeal joint, PIP = proximal interphalangeal joint,
DIP = distal interphalangeal joint, MTP = metatarsophalangeal joint.

Details of the articular involvement of the patients studied are shown in Table 2. The knee was the most commonly affected joint, followed by the ankle, wrist, hip and metatarsophalangeal joints. Spinal pain involving the lumbosacral area was seen in 36 cases (40.9%); it was seen in all JAS cases and all but one of the AS cases. Radiographic bilateral sacroiliitis was seen in all JAS and AS patients and was occasionally seen in RS, PsA, and uSpA. Enthesopathy involving the Achilles tendon and plantar fascia was prominent in JAS, AS, RS, and uSpA patients.

Extra-articular manifestations of these patients are shown in Table 3. Acute inflammatory eye diseases were seen in 5 (45.45%) AS patients and 16 (66.66%) RS patients. Mucocutaneous lesions, genital and oral ulcers, and dysentery were common in patients with RS. None of our RS patients had keratoderma or onychodystrophy. Twelve of 14 patients (85.71%) with PsA had onychodystrophy. Two AS patients who had long standing disease had pulmonary fibrosis. One AS patient who had had the disease for 20 years had an aortic valve replacement because of severe aortic regurgitation.

Four patients were anemic (hematocrit < 30 vol%) at the time of presentation. This was due to gastrointestinal blood loss from non-steroidal anti-inflammatory drug (NSAID) therapy. No patients had significant proteinuria. Two patients had renal impairment (serum creatinine > 1.5 mg/dl), which might have been related to the chronic usage of NSAIDs. Five patients had hypoalbuminemia. RF was negative in all, except one with a low titer (1:40), of those who were tested. Radiographic evidence of involvement of the spine was usually seen in patients with JAS and AS (Table 2).

Table 3. Extra-articular manifestations of Thai patients with spondyloarthropathy.

	Total (n=88)	JAS (n=9)	AS (n=11)	RS (n=24)	PSA (n=14)	uSpA (n=30)
Inflammatory eye diseases						
Conjunctivitis	15	-	2	12	1	-
Uveitis	8	1	3	4	-	-
Keratoderma	-	-	-	-	-	-
Balanitis/genital ulcers	6	-	-	5	1	-
Urethritis/cervicitis	6	-	-	6	-	-
Diarrhea/dysentery	6	-	1	5	-	-
Oral ulcers	2	-	-	2	-	-
Onychodystrophy	12	-	-	-	12	-
Psoriatic skin lesions	14	-	-	-	14	-
Pulmonary fibrosis	2	-	2	-	-	-
Aortic regurgitation	1	-	1	-	-	-

DISCUSSION

The prevalence of SpA has been studied in several countries in Asia. The prevalence of AS has been reported as 0.26 per cent in China[6] (with a prevalence of HLA-B27 of 4%), 0.19-0.54 per cent in Taiwan[7] (HLA-B27 4-8%), 0.15 per cent in Vietnam[8] (HLA-B27 4%), and 0.1 per cent in Iran[9]. A recent study in Thailand[10] (HLA-B27 4%)[11] found a prevalence of all types of SpA of 0.12 per cent. Studies of the HLA subtypes in patients with SpA in Asia have been shown to be associated with HLA-B*2704[12-16], which differs genetically from Caucasians, who carry HLA-B*2705[17,18]. In India and Japan, SpA has been reported to be associated with both HLA-B*2704 and B*2705 subtypes[15,16]. In addition to HLA-B27, HLA-A11 has also been found to be associated with SpA in Thailand[19]. Studies of the HLA-B27 subtypes in Asia have found that the presence of HLA-B*2706 might prevent the development of SpA[14,20]. In Indonesia, Chinese-Indonesians have been shown to have a greater risk of the development of AS and SpA than native Indonesians, despite the lower prevalence of HLA-B27 in Chinese-Indonesians (4% *vs* 9%)[21].

Clinical studies of SpA in Asia are also limited. AS, RS and PsA were the 3 most common types of SpA seen at a university hospital in Thailand[22,23]. The age at onset of these SpA patients was in the third decade. The male to female ratio was higher in patients with AS and RS than in PsA patients. Low back pain was the most common presenting symptom in AS patients, while peripheral arthritis of the lower extremity joints was the most common presenting symptom in RS and PsA patients. Extra-articular features including inflammatory eye diseases, oral and genital ulcers, dysentery, urethritis and balanitis were commonly seen in RS patients. Although a COPCORD study in the Philippines[24] found no cases of AS, a recent survey in the Philippines found 143 patients with SpA. They had ReA and RS in 96 cases, PsA in 26, AS in 17, SpA associated with IBD in 13, uSpA in 10, and juvenile chronic arthritis in 1[25]. Spinal involvement was more common in AS, PsA, and uSpA patients than in ReA and SpA associated with IBD patients. Extra-articular features were also common in RS patients[26]. In Singapore[27] AS was more common in males. The average duration from the onset of symptoms to diagnosis was 7.2 years. Peripheral arthritis occurred in 71 per cent, and 26 per cent of these patients suffered from significant disability. Extra-articular complications were uncommon. A study of PsA in Singapore found that asymmetric peripheral arthritis was the most common presentation[28]. Spondylitis was also common. Kim[29] studied 117 AS patients in Korea and found an average age at diagnosis of 38 years, with a male to female ratio of 9:1. Pulmonary, gastrointestinal and ocular involvement were seen in 29, 15 and 10 per cent of cases respectively. This high incidence of pulmonary involvement differed from previous

reports of SpA from other countries in Asia. In Vietnam[8] AS was seen predominantly in males during the end of the third decade of life. Peripheral arthritis was common, especially in the hip and the knee, which affected 96 per cent and 76 per cent of cases respectively. In northern[30] and southern India[31] AS was seen predominantly in males (male to female ratio of 16:1) with an average age of 25 years. Back pain and oligoarthritis of the lower extremity joints were the most common mode of presentation.

In this study, we found a male to female ratio of 2.2:1 for all types of SpA patients. The ratio was higher in JAS, AS and RS patients. The onset of the disease was in the middle of the third decade of life. Peripheral arthritis was common in all groups while inflammatory back pain and bilateral sacroiliitis were most commonly seen in JAS and AS patients. Extra-articular features were common in RS patients. The clinical features of our SpA patients were similar to those that have been described in other countries in Asia above and western countries[1,2].

It is of interest that up to one third of our patients had uSpA. This group of patients had inflammatory spinal back pain and/or asymmetric oligoarthritis of the lower extremity joints. They did not have extra-articular features of RS or skin lesions that are suggestive of psoriasis. Many of these patients had some evidence of sacroiliitis in the radiographs, but they did not meet the criteria for the diagnosis of AS. This could be because they had not had the disease long enough to have radiographic changes of the sacroiliac joint and the spine that are typical of AS. Mau[5] followed uSpA patients for 10 years and found that 59 per cent of these patients developed definite AS, 19 per cent remained uSpA, and 22 per cent developed other diseases. It might be of interest to follow our patients in this group.

It is now recognized that SpA is probably the most common articular manifestation in patients with HIV infection. SpA associated with HIV infection has been reported to be a more severe, aggressive, and destructive disease, and to respond poorly to NSAIDs[32]. Our experience in patients with SpA associated with HIV infection is that they had a milder clinical course compared with western series, and showed good response to NSAIDs alone[33]. However, up to 75 per cent of our patients did not realize that they had HIV infection at the time of presentation. This is an important point that should be kept in mind: the possibility of HIV infection in SpA patients who have risk factors for this.

In summary, the clinical features of Thai patients with SpA were similar to those reported in western countries and other countries in Asia. USpA was not uncommon, especially in patients who had had the disease for a short time. Whether patients in this group will develop SpA which is more clearly defined remains to be determined.

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การศึกษาลักษณะทางคลินิกของผู้ป่วยสปอนดีย์โลอาร์โธรพาธีย์ในคนไทย

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ได้ทำการศึกษาลักษณะทางคลินิกของผู้ป่วยสปอนดีย์โลอาร์โธรพาธีย์ (SpA) ในคนไทยจำนวน 88 ราย (เพศชาย 61 รายและเพศหญิง 27 ราย) พบว่าอายุและระยะเวลาที่เป็นโรคเฉลี่ยเท่ากับ 25.97 และ 3.34 ปี ตามลำดับ ผู้ป่วย 16 รายมีอาการของโรคก่อนอายุ 16 ปี ในจำนวนผู้ป่วยทั้งหมดแบ่งเป็น ankylosing spondylitis 11 ราย, ankylosing spondylitis ในเด็ก 9 ราย, Reiter's syndrome 20 ราย, Reiter's syndrome ในเด็ก 4 ราย, psoriatic arthritis 14 ราย, undifferentiated SpA 27 ราย และ undifferentiated SpA ในเด็ก 3 ราย ข้ออักเสบไม่กี่ข้อโดยเฉพาะข้อส่วนล่างของร่างกายเป็นอาการนำที่พบได้บ่อยที่สุดในทุกกลุ่มโรค ยกเว้นผู้ป่วย psoriatic arthritis ซึ่งพบข้ออักเสบหลายข้อได้บ่อยกว่า อาการปวดหลังและข้อกระดูกกระเบนเหน็บอักเสบพบได้บ่อยในผู้ป่วย ankylosing spondylitis ทั้งในผู้ใหญ่และเด็ก ภาวะ enthesopathy พบได้บ่อยเช่นกัน อาการแสดงนอกระบบข้อพบได้บ่อยในผู้ป่วย Reiter' syndrome ร้อยละ 45 ของผู้ป่วย ankylosing spondylitis และร้อยละ 66 ของผู้ป่วย Reiter's syndrome มีตาอักเสบ ลักษณะทางคลินิกของผู้ป่วย spondyloarthropathy ในคนไทยคล้ายกับที่เคยมีรายงานจากประเทศในทวีปเอเชียและประเทศทางตะวันตก

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