Sensitivity and specificity of criteria for spondyloarthritis in children with late onset pauciarticular juvenile chronic arthritis as well as their characteristics

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Abstract

Objective

To evaluate the sensitivity and specificity of criteria designed for spondyloarthritis in a university hospital treated population of children with late onset pauciarticular juvenile chronic arthritis and a control population.

Methods

Four sets of criteria especially designed for juvenile patients: Garmisch-Partenkirchen juvenile spondylitis criteria (= Garmisch), SEA (=seronegative enthesopathy and arthritis) syndrome, Enthesitis Related Arthritis (ERA), Atypical spondyloarthritis for children and two sets of criteria for patients without age specification (European spondyloarthropathy Study Group – ESSG and Amor) were evaluated in a cross-sectional way in a group of 43 consecutive patients with late onset pauciarticular juvenile chronic arthritis (LOPA) seen over a six-month period in the outpatient clinic. These criteria were analysed in 69 patients with other forms of juvenile chronic arthritis as well. The sensitivity and specificity were calculated for each set, as well as positive predictive value and likelihood ratio. The characteristics described in the different sets of criteria were separately evaluated in the LOPA patients and the other patients.

Results

For sensitivity, the Garmisch criteria scored the highest value (97.7%). However, sensitivity was significantly lower in two of the juvenile sets (SEA syndrome and Atypical spondyloarthritis), respectively 44.2% and 51.2%, as opposed to the other criteria (>85%; p<0.01 by Mc Nemar test). Specificity and positive predictive value (PPV) was the highest for the SEA syndrome criteria (98.5%, vs. 95.0%) followed by the ERA (95.6 % vs. 92.1 %) and the Garmisch criteria (94.2% vs. 91.3%). The positive likelihood ratio (LR+) was >10 in SEA (30.5), ERA (18.7) and Garmisch (16.8). The negative likelihood ratio (LR-) was <0.1 only in the Garmisch criteria (0.02).

Conclusion

Sensitivity, specificity, PPV, LR+ and LR- for the Garmisch-Partenkirchen criteria suggest that they classify almost the same population as defined by LOPA. The SEA syndrome criteria, which were not designed to be classification criteria, being very specific, cannot be used in this patient population to classify a sufficient number of patients. The sensitivity and specificity for the ESSG criteria being similar in these children as in adults suggest they have similar characteristics. The Garmisch-Partenkirchen criteria and/or LOPA definition are major candidates for future research in identifying spondyloarthritis in juvenile patients.

Key words

Criteria, spondyloarthritis, characteristics in children.

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Introduction

Spondyloarthritis refers to a group of diseases sharing common characteristics such as the absence of rheumatoid factor or nodules, the presence of a peripheral oligoarthritis essentially with an asymmetrical pattern and especially involving the lower limbs, occurrence of sacroiliitis with or without spondylitis, presence of enthesitis, familial aggregation with occurrence of the different diseases of the group in the same family and an association with HLA B27.

More and more awareness of the existence of spondyloarthritis in children rises. (1-5) but convincing information about the value of different sets for classification lacks.

Some years ago attempts have been made to come to a concept of spondyloarthritis in children describing some characteristics of this group of diseases that seemed distinct from other patients with juvenile inflammatory rheumatic diseases (6).

Others identified a group of children with clinical characteristics of ankylosing spondylitis or resembling spondyloarthritis. This entity was called the SEA syndrome (7). In the classification of juvenile rheumatoid arthritis (JRA) (8), the juvenile ankylosing spondylitis was excluded meaning that it was considered to be separate from the other forms of JRA.

The European classification of the juvenile chronic arthritis (JCA) (9) does not exclude the spondyloarthritides or the juvenile ankylosing spondylitis. Studies have demonstrated similar characteristics in patients suffering from late onset pauciarticular JCA and in undifferentiated spondyloarthritis of the adult.(10, 11). The late onset pauciarticular juvenile chronic arthritis is characterized by a chronic (>3 months duration) asymmetrical oligoarthritis, predominantly of the lower limbs, with or without enthesitis, occurring in children of 10 years or more, mainly boys and associated with a high prevalence of HLA B27 and possible occurrence of an acute anterior uveitis (9).

We studied a group of children fitting into the classification of "the late onset pauciarticular juvenile chronic arthritis (LOPA)". This group was chosen because in our point of view the patients resembled the most the characteristics of spondyloarthritis as defined by the European Spondyloarthropathy Study Group (12). Consequently, we were forced to consider control patients with other forms of juvenile chronic arthritis, although this nomenclature is practically out of use in daily practice.

The more recent juvenile idiopathic arthritis (JIA) nomenclature (13, 14) could not be used since the point of departure is located in the JCA classification and is compared (amongst others) to the enthesitis related arthritis (ERA), a subgroup of JIA patients.

The objective of this paper was to test several sets of criteria meant to identify spondyloarthritides or spondyloarthritis like diseases on their specificity and sensitivity in children with LOPA.

Patients and methods

Patients

Forty-three consecutive patients attending the outpatient clinic of the centre of paediatric and adolescent rheumatology in a six-month period who were diagnosed as "late onset pauciarticular juvenile chronic arthritis" (LOPA) (9) were evaluated in a cross sectional way. Three of the six described characteristics of LOPA (asymmetrical oligoarthritis, enthesitis, male, onset >10 years, HLA B27 positive, acute anterior uveitis) had to be present to include the patient in this study.

The clinical evaluation (interrogatory, physical exam) of the patients was carried out by R. Joos, J. Dehoorne and D. Elewaut. Laboratory testing was done routinely in all patients, including HLA testing. x-rays of the lumbar spine and sacroiliac joints were only performed when inflammatory low back pain was present.

Controls

Sixty-nine consecutive patients with other forms of juvenile chronic arthritis attending the same outpatients clinic were evaluated with the same methodology. The ratio patients/controls reflects the frequency of the late onset pauciarticular juvenile chronic arthritis in our patients population.

Criteria

Six sets of criteria – listed below – were evaluated :

- European Spondylarthropathy Study Group criteria for the classification of spondyloarthropathy (12) (ESSG);
- Amor criteria for the classification of spondyloarthropathy (15)
- SEA syndrome (7)
- Enthesitis Related Arthritis (ERA) (14)
- Atypical spondyloarthritis in children (16)
- Garmisch-Partenkirchen juvenile spondylitis criteria ("probable spondylitis" set) (17).

Four sets of criteria were designed especially for children, (7, 14, 16, 17) the other two sets were designed for adults (12, 15).

For the purpose of the readers these criteria are made available as an addendum.

Methods

We conducted a cross sectional analysis of the medical records of the patients evaluating the fulfilment of six sets of criteria for spondyloarthritis mentioned above. For that purpose approval by the ethical committee was obtained.

For the statistical analysis, sensitivity, specificity, positive and negative predictive value and likelihood ratios of the criteria were calculated . For the individual items of the different criteria the chi square test was used to demonstrate whether an individual item discriminated between the LOPA group and the controls. $p<0.05$ was considered statistically significant. The comparison of sensitivities and specificities of the criteria was calculated by means of the McNemar test.

Results

The patient population consisted of 43 consecutive patients with late onset pauciarticular juvenile chronic arthritis (LOPA) seen in a six month period. Twenty two of them were males and 21 females. All patients were Caucasian. The mean age at onset was 10.5 years (SD 3.1 years). The duration of disease ranged from 7 months to 144 months with a median of 29 months. The mean age of the patients at the time of evaluation was 13.9 years (SD 4.1 years).

In the control population 21 of the 86 patients were males. 41 patients were diagnosed as having early onset pauciarticular arthritis (EOPA) and 25 suffered from polyarticular juvenile chronic arthritis. Three patients suffered from systemic onset JCA with persistent arthritis and the remaining patients suffered from other inflammatory auto-immune diseases.

We evaluated the fulfilment of all the different items from the various sets of classification criteria in patients with LOPA and controls. Table I describes the absolute and relative frequency among these two groups for each of these items.

Inflammatory spinal pain occurred in 23 patients with LOPA compared to only 14 controls ($p<0.05$). An asymmetrical oligoarthritis was observed in 38 patients as opposed to 24 controls ($p<0.05$). Hip arthritis did not discriminate between LOPA patients and controls. HLA B27 was found to be present in 25 patients with LOPA but only in

ESSG criteria (12)

Inflammatory low back pain	AND at least one of the following criteria
OR	- familial history of spondyloarthropathy, uveitis or inflammatory bowel disease
Synovitis asymmetrical or predominantly of the lower limbs	- psoriasis - inflammatory bowel disease - enthesopathy - radiological sacroiliitis

Amor criteria (15)

		Points
A. Clinical signs or history of		
	1. nocturnal pain lumbar or dorsal and/or morning stiffness lumbar dorsal	1
	2. asymmetrical oligoarthritis	2
	3. indefinite buttock pain	1
	or alternating buttock pain	or 2
	4. sausage finger or toe	2
	5. heelpain or any other enthesopathy	2
	6. iritis	2
	7. non gonococcal urethritis or cervicitis within one month before the onset of the arthritis	1
	8. diarroea within one month before the onset of the arthritis	1
	9. presence or history of psoriasis, and/or balanitis and/or chronic enterocolopathy	2
B. Radiological signs		
	10. sacroiliitis (stade 2 ≥ if bilateral, or stade ≥ 3 if unilateral)	3
C. Genetics		
	11. presence of HLA B27 and/or familial history of ankylosing spondylitis and/or Reiter's syndrome and/or psoriasis and/or uveitis and/or chronic enterocolopathy	2
D. Reaction to treatment		
	12. improvement of pain within 48 hours by NSAIDs or relapse within 48 hours after stop of NSAIDs	2

A spondyloarthropathy is declared in a patient having a score equal or greater than 6 as a sum of the points on the 12 criteria.

SEA syndrome (7)

Seronegativity	= absence of rheumatoid factor and antinuclear antibodies
Enthesopathy	= tendonitis of the achillestendon, fascia plantaris or quadricepstendon
Arthropathy	= inflammatory arthritis of the axial skeleton or an oligoarthropathy

Enthesitis related arthritis – Durban criteria (14).

1. **Arthritis OR Enthesitis**

2. **PLUS two or more of the following**
   - A. sacroiliac joint tenderness AND/OR inflammatory spinal pain
   - B. presence of HLA-B27
   - C. family history involving one or more first or second degree relatives with an HLA-B27 related disease, confirmed by a physician
   - D. anterior uveitis (typically with pain, redness and/or photophobia)
   - E. onset of arthritis in a boy > 8 years of age

3. **AND none of the following**
   - A. presence of psoriasis in a first or second degree relative, confirmed by a dermatologist
   - B. presence of a systemic arthritis.

Atypical spondyloarthritis in children (16).

Major criteria
1. SA or oligoarthritis in the family
2. enthesopathy
3. arthritis of digital joints
4. sacroiliitis
5. HLA B27 positive
6. recurrent arthritis or arthralgia

Minor criteria
1. Begin after age of 10 years
2. male sex
3. only lower extremities affected
4. acute iridocyclitis or conjunctivitis
5. arthritis of hips
6. begin following an unproven enteritis

Atypical spondyloarthritis was considered as probable when three major and two minor criteria were present.

Juvenile spondarthritis (Garmisch-Partenkirchen criteria) (17).

Major criteria
1. asymmetrical oligoarthritis with involvement of hip, knee or ankle joint
2. enthesopathy
3. pain of the lumbar spine or the sacroiliac region
4. acute iridocyclitis

Minor criteria
1. peripheral arthritis of 5 or more joints
2. male sex
3. disease onset after the age of 6 years
4. HLA B27 positivity
5. (suspicion of) spondarthritis in the family history

Probable spondarthritis was considered if two major criteria or major criterion one or two plus two minor criteria were present.

one control patient ($p<0.05$). A positive family history for other diseases of the spondyloarthritis group was present in 33 LOPA patients versus 3 control patients ($p<0.05$).

Sensitivity and specificity were calculated for each set in the patient group and the control population. The results are illustrated in Table II.

The highest sensitivity was obtained by the Garmisch-Partenkirchen criteria, while ESSG, Amor and ERA had a sensitivity of more than 80% of the patients. The sensitivity of the SEA syndrome criteria and the criteria for atypical spondyloarthritis in children appeared to be markedly lower than the other criteria ($p<0.01$ by McNemar test). The specificity of all examined criteria appeared to be rather high (>85%); the highest for SEA; the lowest for ESSG ($p<0.01$ by McNemar test). Positive predictive value was again the highest for SEA, while the highest value for negative predictive value was obtained by the Garmisch criteria. A positive likelihood ratio of >10 was obtained by SEA, ERA and Garmisch, while a negative likelihood ratio <0.1 was only achieved by the Garmisch criteria.

Discussion

Our objective was to evaluate the sensitivity, specificity and characteristics of six sets of criteria (7, 12, 14-17) for spondyloarthritides or similar diseases in a patient population suffering from late onset pauciarticular juvenile chronic arthritis and to compare the results with a parallel evaluation in another patient population suffering from other forms of juvenile chronic arthritis. Because the clinical characteristics of the late onset pauciarticular juvenile chronic arthritis (LOPA) resembled the most the characteristics of the spondyloarthritis definition for adults (12, 15), this group was used as the basis for selection of the studied patient population. Moreover, some studies confirmed that besides the clinical characteristics other features were similar to the adult spondyloarthritis. The frequency of HLA B27 (16, 18, 19) and the association with bowel inflammation (10, 11) as well as the association with acute anterior uveitis (20, 21) were previously described. In this study the most discriminating characteristics between LOPA and other patients were similar as previously described. (axial inflammatory involvement, asymmetrical oligoarthritis of the lower limbs, enthesitis, acute anterior uveitis, psoriasis, male sex, rheumatoid factor, absence of antinuclear antibodies , “older age” at onset, family history, HLA B27 presence).

Children presenting with undifferentiated forms of juvenile onset spondyloarthritis often progressed to differentiated forms over time. (22) Moreover, several patients evolved towards adult forms of spondyloarthritis and even ankylosing spondylitis. This is consistent with the findings in the original series of patients described as SEA syndrome, with a higher frequency of spondyloarthritis (52%) after a mean follow up of 11 years (23). A long term (15 and 23 years after disease onset) follow-up study in patients with enthesitis related arthritis in Norwegian patients showed

Table I. Fulfilment of the different characteristics of the various sets of classification criteria evaluated in the studied patient cohort.

Frequency	Patients (n=43)	%	Controls (n=69)	%	χ^2	*p*-value
Axial involvement						
Inflammatory spinal pain	23	53.5	9	13.0	19.3	<0.05
Lumbar or thoracic pain or stiffness	17	39.5	8	11.6	10.4	<0.05
Sacroiliac pain	4	9.3	0	0	4.2	NS
Lumbar or sacroiliac pain	15	34.9	7	10.1	8.8	<0.05
Radiographic lesions of the axial skeleton	3	7.0	0	0	2.6	NS
Sacroiliitis	5	11.6	0	0	5.9	<0.05
Peripheral involvement						
Arthralgia or arthritis	43	100	69	100	0	NS
Synovitis, asymmetrical or predominantly lower limbs	40	93.0	53	76.8	3.8	NS
Involvement of lower limbs	39	90.7	53	76.8	2.6	NS
Asymmetrical oligoarthritis	38	88.4	24	34.8	28.6	<0.05
Oligoarthritis in the first three months	36	83.7	45	65.2	3.6	NS
Arthritis in > =5 joints in the first three months	7	16.3	23	33.3	3.1	NS
Arthritis of digits	17	39.5	17	24.6	2.1	NS
Hip arthritis	9	20.9	10	14.5	0.4	NS
Sausage toe	2	4.6	0	0	1.1	NS
Enthesitis/enthesopathy	22	51.2	1	1.4	37.1	<0.05
Family history and HLA B27						
Family history or HLA B27	39	90.7	4	5.8	77.2	<0.05
Family history	33	76.7	3	4.3	60.4	<0.05
Spondyloarthritis in family	29	67.4	2	2.9	51.9	<0.05
HLA B27	25	58.1	1	1.4	44.6	<0.05
Extra-articular involvement						
Psoriasis	7	16.3	0	0	9.3	<0.05
Psoriasis – balanitis – chronic enterocolitis	7	16.3	0	0	9.3	<0.05
IBD	2	4.6	0	0	1.1	NS
Diarrhoea <1 month	2	4.6	0	0	1.1	NS
Urethritis – cervicitis or acute diarrhoea < 1 month	3	7.0	0	0	2.6	NS
Symptoms of enteritis	2	4.6	0	0	1.1	NS
Urethritis – cervicitis < 1 month	1	2.3	0	0	0.1	NS
Iritis	4	9.3	11	15.9	0.5	NS
Anterior uveitis	3	7.0	5	7.2	0.1	NS
Acute iridocyclitis or conjunctivitis	5	11.6	0	0	5.9	NS
Demography						
Start <17 y	43	100	69	100	0	NS
Start >10 y	25	58.1	14	20.3	15.1	<0.05
Onset >6 y	38	88.4	28	40.6	23.1	<0.05
Male sex	22	51.2	12	17.4	12.7	<0.05
Various						
Good effect of NSAID	22	51.2	26	37.7	1.4	NS
RF and ANA negative	38	88.4	20	29.0	35.1	<0.05

The items were filled in as defined by the designers of the criteria.

reduced spinal flexion in 75% and sacroiliitis in 35% (24).

Of the six sets of criteria we considered, four sets were especially designed for children (7, 14, 16, 17) and two sets that were developed in an adult population (12, 15).

In the validation of these sets of criteria in a population of patients with late onset pauciarticular juvenile chronic arthritis, the highest score for sensitivity and a very high score for specificity in patients with late onset pauciarticular juvenile chronic arthritis was obtained by the Garmisch-Partenkirchen criteria (17). For the positive and negative predictive value, as well as for the positive and negative likelihood ratio these criteria obtained strong scores. None of the other sets obtained sufficient scores on the different tests, lacking sensitivity (SEA, Atypical), not showing enough positive predictive value (ESSG, Atypical), insufficient negative predictive value (SEA, atypical), too low positive likelihood ratio (ESSG, Amor, Atypical), too high negative likelihood ratio (ESSG, Amor, SEA, ERA, Atypical).

Sensitivities and specificities are concordant with the results in a group of Turkish patients, although the authors started from a empiric definition of juvenile spondyloarthritis including juvenile ankylosing spondylitis, reactive arthritis, juvenile psoriatic arthritis, arthritis associated with inflammatory bowel disease and undifferentiated spondyloarthopathies (25). The sensitivity and specificity found for children

Table II. Evaluation of six sets of criteria in patients with late onset pauciarticular juvenile chronic arthritis and control patients at the moment of diagnosis.

	ESSG	AMOR	SEA	ERA	Atypical	Garmisch
LOPA	37/43	37/43	19/43	35/43	22/43	42/43
Control	10/69	6/69	1/69	3/69	7/69	4/69
Sensitivity (%)	86.0	86.0	44.2	81.4	51.2	97.7
Specificity (%)	85.5	91.3	98.5	95.6	89.8	94.2
PPV (%)	78.7	86.0	95.0	92.1	75.8	91.3
NPV (%)	90.8	91.3	73.9	89.2	74.7	98.5
LR+	5.9	9.9	30.5	18.7	5.0	16.8
LR–	0.16	0.15	0.57	0.19	0.54	0.02

LOPA: late onset pauciarticular juvenile chronic arthritis (9); CONTROL: control patients = patients with other forms of juvenile inflammatory rheumatic diseases; ESSG: European Spondyloarthropaty Study Group criteria for the classification of spondyloarthropathy (12); AMOR: Amor criteria for the classification of spondyloarthropathy (15); SEA: SEA syndrome (7); ERA: Enthesitis related arthritis (14); Atypical: Atypical spondyloarthritis in children (16); Garmisch: Garmisch-Partenkirchen juvenile spondylitis criteria (17); PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio; LR–: negative likelihood ratio.

with late onset pauciarticular juvenile chronic arthritis for the ESSG criteria are almost identical to those found in adults with spondyloarthritis (12) suggesting that LOPA can be considered as part of the spondyloarthritis concept.

Designing criteria especially for children can increase the quality of classification criteria for spondyloarthritis as is shown for the Garmisch-Partenkirchen criteria (17). These criteria were constructed through a retrospective analysis of the characteristics of 71 patients who had developed a radiographic sacroiliitis. From these characteristics, a set of disease specific characteristics (major criteria) was distilled as well as a set of characteristics (minor criteria) found also in other HLA B27 associated diseases such as psoriatic arthritis, arthritis associated with inflammatory bowel disease or chronic Reiter's syndrome. The lack of a control group as well as the lack of statistical analysis compromise the construct validity of these criteria.

In earlier studies the two sets of criteria designed for adults (ESSG, Amor) were found to be applicable in children to identify a group of spondyloarthritis (26, 27).

Yet in this group of children with LOPA they proved to be far less performing than the Garmisch-Partenkirchen criteria.

The heterogeneity of the different sets of criteria, the unsatisfactory scores of the adult sets and the limited spread and use of some specific sets designed for children incite us to aim for the construction of a world wide acceptable set of classification criteria for children with spondyloarthritis. Since the Garmisch-Partenkirchen criteria obtained top scores as well for specificity as for sensitivity, PPV, NPV, LR + and LR, it seems that they cover almost the same target population as defined by the late onset pauciarticular juvenile chronic arthritis.

Moreover, it is mandatory that the paediatrician's and the rheumatologist's approach to these patients becomes more uniform. Therefore, both specialties should agree on a common strategy, defining the characteristics of the patients with presumed juvenile spondyloarthritis.

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References

1. HOFER M: Spondylarthropathies in children – are they different from those in adults? *Best Pract Res Clin Rheumatol* 2006; 20: 315-28.
2. MALLESON PN, PETTY RE: Clinical and therapeutic aspects of juvenile-onset spondyloarthropathies. *Curr Opin Rheumatol* 1997; 9: 291-4.
3. BURGOS-VARGAS R, RUDWALEIT M, SIEPER J: The place of juvenile onset spondyloarthropathies in the Durban 1997 ILAR classification criteria of juvenile idiopathic arthritis. International League of Associations for Rheumatology. *J Rheumatol* 2002; 29: 869-74.
4. GARCÍA-CONSUEGRA MOLINA J, MERINO MUÑOZ R, FERNÁNDEZ REVUELTA S, SOLER BALDA C: Juvenile spondyloarthropathies: descriptive study of 40 patients. *An Esp Pediatr* 1998; 48: 489-94.
5. ROSENBERG AM: Juvenile onset spondyloarthropathies. *Curr Opin Rheumatol* 2000; 12: 425-9.
6. VEYS EM, MIELANTS H, JOOS R, DE CLERCQ L: Juvenile spondyloarthropathies in 1992. *J Rheumatol* 1993; 20 (Suppl. 37): 19-25.
7. ROSENBERG AM, PETTY RE: A syndrome of seronegative enthesopathy and arthropathy in children. *Arthritis Rheum* 1982; 25: 1041-7.
8. BREWER EJ, BASS J, BAUM J *et al.*: Current proposed revision of JRA criteria. A*rthritis Rheum* 1977; 20 (Suppl. 2): 195-9.
9. WOOD PHN: Nomenclature and classification of arthritis in children. *In* E. MUNTHE (Ed.) *The care of rheumatic children*, EULAR, Basel 1978; 47.
10. MIELANTS H, VEYS EM, JOOS R, CUVELIER C, DE VOS M, PROOT F: Late onset pauci-articular juvenile chronic arthritis: relation to gut inflammation. *J Rheumatol* 1987; 14: 459-65.
11. MIELANTS H, VEYS EM, CUVELIER C *et al.*: Gut inflammation in children with late onset pauciarticular juvenile chronic arthritis and evolution to adult spondyloarthropathy - A prospective study. *J Rheumatol* 1993; 20: 1567-72.
12. DOUGADOS M, VAN DER LINDEN S, JUHLIN R *et al.*: The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. *Arthritis Rheum* 1991; 34: 1218-27.
13. FINK CW: Proposal for the development of classification criteria for idiopathic arthritides of childhood. *J Rheumatol* 1995; 22: 1566-9.

14. PETTY RE, SOUTHWOOD TR, BAUM J *et al*.: Revision of the proposed classification criteria for juvenile idiopathic arthritis: Durban 1997. *J Rheumatol* 1998; 25: 1991-4.
15. AMOR B, DOUGADOS M, LISTRAT V *et al*.: Evaluation des critères de spondylarthropathies d'Amor et de l'European Spondylarthropathy Study Group (ESSG). Une étude transversale de 2228 patients. *Ann Med Interne* (Paris) 1991; 142: 85-9.
16. HUSSEIN A, ABDUL-KHALIQ H, VON DER HARDT H: Atypical spondyloarthritis in children: proposed diagnostic criteria. *Eur J Pediatr* 1989; 14: 513-7.
17. HÄFNER R: Die Juvenile Spondylarthritis. Retrospektive Untersuchung an 71 Patienten. *Monatsschr Kinderheilkd* 1987; 135: 41-6.
18. CALIN A: Ankylosing Spondylitis. *In* WN KELLEY, ED HARRIS, S RUDDY, CG SLEDGE (Eds.) *Textbook of rheumatology,* 3rd edn. W.B. Saunders, Philadelphia, p.1021-37.
19. EDMONDS J, MORRIS RI, METZGER AL *et al*.: Follow-up study of juvenile chronic polyarthritis with particular reference to histocompatibility antigen W27. *Ann Rheum Dis* 1974; 33: 289-92.
20. VEYS EM, COIGNÉ E, MIELANTS H, VERBRUGGEN A: HLA and juvenile chronic polyarthritis. *Tissue Antigens* 1976; 8: 61-5.
21. SCHALLER JG: Ankylosing spondylitis of childhood onset. *Arthritis Rheum* 1977; 20: 398-401.
22. BURGOS-VARGAS R, VAZQUEZ-MELLADO J: The early clinical recognition of juvenile-onset ankylosing spondylitis and its differentiation from juvenile rheumatoid arthritis. *Arthr Rheum* 1995; 38: 835-44.
23. CABRAL DA, OEN KG, PETTY RE: SEA syndrome revisited: a longterm follow up of children with a syndrome of seronegative enthesopathy and arthropathy. *J Rheum* 1992; 19: 1282-5.
24. FLATØ B, HOFFMANN-VOLD AM, REIFF A, FØRRE Ø, LIEN G, VINJE O: Long-term outcome and prognostic factors in enthesitis-related arthritis: a case control study. *Arthritis Rheum* 2006; 54: 3573-82.
25. KASAPCOPUR O, DEMIRLI N, OZDOGAN H *et al*.: Evaluation of classification criteria for juvenile-onset spondyloarthropathies. *Rheumatol Int* 2005; 25: 414 -8.
26. PRIEUR AM: Spondyloarthropathies in children. *Ann Med Interne* (Paris) 1998; 149: 156-8.
27. PRIEUR AM: Spondyloarthropathies in childhood. *Baillières Clin Rheumatol* 1998; 12: 287-307.