The Influence of Heredity for Psoriasis on the ILAR Classification of Juvenile Idiopathic Arthritis

LILLEMOR BERNTSON, ANDERS FASTH, BOEL ANDERSSON-GÄRE, TROELS HERLIN, JON KRISTINSSON, PEKKA LAHDENNE, GUDMUND MARHAUG, SUSAN NIELSEN, PIRKKO PELKONEN, MARITE RYGG, for THE NORDIC STUDY GROUP

ABSTRACT. ***Objective.*** To evaluate how heredity for psoriasis influences classification according to the International League of Associations for Rheumatology (ILAR). Heredity for psoriasis is currently both an exclusion and an inclusion criterion for different types of childhood arthritis according to ILAR classification criteria.

Methods. Twenty physicians in 5 Nordic countries prospectively collected data from the incident cases in their catchment areas over an 18 month period beginning July 1, 1997. Clinical and serological data from the first year of disease were collected.

Results. Of the 321 patients included who could be classified according to ILAR criteria for childhood arthritis, 50 (15.6%) patients were excluded from 55 classification events and fulfilled criteria for "other arthritis 1" i.e., did not fulfill criteria for any of the other classification categories, primarily because of heredity for psoriasis. If psoriasis in second degree relatives was disregarded as an exclusion criterion, only 8.7% of the patients remained in the "other arthritis 1" subgroup. For 20.6% of the whole group, heredity for psoriasis in a first or second degree relative (or both) and its distribution among arthritis subgroups did not differ except for juvenile psoriatic arthritis.

Conclusion. We suggest that second degree heredity for psoriasis be withdrawn as an exclusion criterion from the ILAR criteria. (J Rheumatol 2002;29:2454–8)

Key Indexing Terms:
ARTHRITIS JUVENILE RHEUMATOID ARTHRITIS
CLASSIFICATION CHILD HEREDITY

Pediatric rheumatologists have long demanded a unified classification of childhood arthritis[1]. Classification of a disorder is necessary to keep information manageable and applicable especially in research[2].

From the Department of Pediatrics, Falun Hospital and Göteborg University, Göteborg and the Department of Pediatrics, Ryhov Hospital, Jönköping, Sweden; the Department of Pediatrics, Skejby Hospital, Århus, Denmark; the Department of Pediatrics, Landspitalinn, Reykjavik, Iceland; the Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland; the Department of Pediatrics, Hospital of Trondheim, Norway; and the University Clinic of Pediatrics II, Rigshospitalet, Copenhagen, Denmark.

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L. Berntson, MD, Consultant in Pediatrics, Department of Pediatrics, Falun Hospital and Göteborg University; A. Fasth, MD, PhD, Professor in Pediatric Immunology, Department of Pediatrics, Göteborg University; B. Andersson-Gäre, MD, PhD, Physician-in-Chief, Department of Pediatrics, Ryhov Hospital; T. Herlin, MD, PhD, Skejby Hospital; J. Kristinsson, MD, Consultant in Pediatrics, Department of Pediatrics, Landspitalinn; P. Lahdenne, MD, PhD, Hospital for Children and Adolescents, University of Helsinki; G. Marhaug, Professor, Department of Pediatrics, Hospital of Trondheim; S. Nielsen, MD, University Clinic of Pediatrics II, Rigshospitalet; P. Pelkonen, MD, PhD, Hospital for Children and Adolescents, University of Helsinki; M. Rygg, MD, PhD, Department of Pediatrics, Hospital of Trondheim.

Address reprint requests to Dr. L. Berntson, Department of Pediatrics, Falun Hospital, SE -79182 Falun, Sweden.
E-mail: lillemor.berntson@falun.mail.telia.com

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In the most recently proposed classification system by the International League of Associations for Rheumatology (ILAR), heredity for psoriasis plays an important role[3]. Heredity for psoriasis in a first or second degree relative is an exclusion criterion for oligoarthritis and enthesitis-related arthritis. Psoriasis is well known to predispose for arthritis[4-6]. The disposition is evident both in patients with arthritis with psoriasis and in relatives of patients with psoriasis. Recent studies on ILAR classification have shown a high frequency of patients being classified as "other arthritis 1", i.e., fitting no category, because of psoriasis in first or second degree relatives[7-9]. Our aim was to study the influence of heredity for psoriasis in ILAR classification in our prospective, population based cohort of patients. Another aim was to evaluate the impact of first degree heredity for psoriasis on type of onset in oligoarthritis as well as other features, such as the distribution of psoriasis heredity among ILAR subgroups.

MATERIALS AND METHODS

Data collection. Twenty pediatricians with experience in pediatric rheumatology in 5 Nordic countries prospectively collected data from the incident cases in their catchment areas during an 18 month period beginning July 1, 1997. Clinical and serological data from the first year of the disease were collected.

Classification of the patients according to the ILAR/Durban criteria[3] and the Vancouver criteria[10,11] was performed by the coordinator of the study at 6 months' disease duration and in some cases at one year

(oligoarthritis, persistent or extended). Ten of the patients with oligoarthritis could not be classified as persistent or extended because they dropped out of followup after 6 months of disease. For the present study, classification was repeated for the whole group of 321 patients without second degree heredity for psoriasis as an exclusion criterion.

The seventh category of the ILAR classification, "other arthritis", consists of 2 subdivisions: "other arthritis 1", which accommodates children who do not fulfill criteria for any of the other categories, and "other arthritis 2", for children fulfilling criteria for more than one of the other categories (Table 1). For patients who belong to "other arthritis 2", we called each classification a classification event.

As mentioned above, another set of criteria for juvenile psoriatic arthritis, the Vancouver criteria[10], was also used. In the Vancouver criteria "definite juvenile psoriatic arthritis" is defined as arthritis beginning before age 16, typical psoriasis or arthritis, and 3 of the following: (1) dactylitis, (2) nail pitting, (3) psoriasis-like rash, and (4) family history of psoriasis (first or second degree relative). "Probable juvenile psoriatic arthritis" was defined as arthritis plus 2 of the minor criteria described above.

Patients with oligoarthritis with and without first degree relatives with psoriasis were compared. The following 4 variables were analyzed: extended or persistent pattern of arthritis, ANA (positive or negative), HLA-B27 (positive or negative), and uveitis (onset or not during the first 6 months of disease). We included all patients with a clinical picture of oligoarthritis in the comparison, not only those fulfilling the ILAR criteria for the 2 oligoarthritis subgroups. Consequently patients belonging to the oligoarthritis persistent subgroup (n = 122), the oligoarthritis extended subgroup (n = 17), the group of patients having an oligoarthritis not classified (n = 10), oligoarthritis as one of 2 diagnoses (n = 9) and the patients having oligoarthritis but who were excluded mainly because of heredity for psoriasis (n = 50) were all considered to have oligoarthritis in this comparison.

Table 1. ILAR criteria definitions and exclusions.

Systemic arthritis
Definition. Arthritis with or preceded by daily fever of at least 2 weeks duration, that is documented to be quotidian for at least 3 days and accompanied by one or more of the following
- a) Evanescent, non-fixed erythematous rash
- b) Generalized lymph node enlargement
- c) Hepatomegaly or splenomegaly
- d) Serositis

Exclusions have not been listed.

Oligoarthritis
Definition. Arthritis affecting 1–4 joints during the first 6 months of disease. Two subcategories are recognized:
- a) Persistent oligoarthritis: affects no more than 4 joints throughout the disease course
- b) Extended oligoarthritis: affects a cumulative total of 5 joints or more after the first 6 months of disease

Exclusions
- a) Family history of psoriasis confirmed by a dermatologist in at least one first or second degree relative
- b) Family history consistent with medically confirmed HLA–B27 associated disease in at least one first or second degree relative
- c) Positive RF test
- d) HLA–B27 positive male with onset of arthritis after 8 years of age
- e) Presence of systemic arthritis as defined above

Polyarthritis (RF negative)
Definition. Arthritis affecting 5 or more joints during the first 6 months of disease, associated with negative RF tests on 2 occasions at least 3 months apart.
Exclusions
- a) Presence of RF
- b) Presence of systemic arthritis as defined above

Polyarthritis (RF positive)
Definition. Arthritis affecting 5 or more joints during the first 6 months of disease, associated with positive RF tests on 2 occasions at least 3 months apart.
Exclusions
- a) Absence of positive tests for RF on 2 occasions at least 3 months apart
- b) Presence of systemic arthritis as defined above

Psoriatic arthritis
Definition
1. Arthritis and psoriasis OR
2. Arthritis and at least 2 of:
   - a) Dactylitis
   - b) Nail pitting or onycholysis
   - c) Family history of psoriasis confirmed by dermatologist in at least one first degree relative

Exclusions
- a) Presence of rheumatoid factor
- b) Presence of systemic arthritis as defined above

Enthesitis-Related Arthritis
Definition.
1. Arthritis and enthesitis OR
2. Arthritis or enthesitis with at least 2 of
   - a) Sacroiliac joint tenderness and/or inflammatory spinal pain
   - b) Presence of HLA-B27
   - c) Family history in at least one first or second degree relative of medically confirmed HLA-B27 associated disease
   - d) Anterior uveitis that is usually associated with pain, redness, or photophobia
   - e) Onset of arthritis in a boy after the age of 8 years

Exclusions
- a) Psoriasis confirmed by a dermatologist in at least one first or second degree relative
- b) Presence of systemic arthritis as defined above.

Other Arthritis
Definition. Children with arthritis of unknown cause that persists for at least 6 weeks but that either
- a) Does not fulfil criteria for any of the other categories, or
- b) Fulfills criteria for more than one of the other categories.

Exclusions
- a) Patients who meet criteria for other categories

Serology. ANA or RF positivity were defined in accordance with the ILAR classification. Thus 2 positive analyses are required with at least 3 months in between. If 2 analyses were made and the result was one positive and one negative, data were defined as not conclusive. The result of RF analysis is also described in cases when RF was analyzed.

Ethics. Informed consent was obtained from both parents and children. The Research Ethical Committees at each regional university gave their approval.

Statistical methods. Fisher's exact test was used to compare onset type between patients with oligoarthritis with first grade heredity for psoriasis versus those without.

RESULTS

A total of 321 patients classified according to the ILAR criteria were included. The ILAR subgroups and exclusion criteria are presented in Table 1, and the results of ILAR classification in Table 2. Ten patients (10/321), 3.1%, had psoriatic arthritis according to the ILAR criteria, 5 patients (5/321), 1.6%, were classified as definite psoriatic arthritis and 5 (5/321), 1.6%, as probable psoriatic arthritis according to the Vancouver criteria. In 5 of the 10 children with psoriatic arthritis according to the ILAR criteria, psoriasis was diagnosed before arthritis or during the first 6 months of disease. In the other 5, the diagnosis was based on nail pitting and first degree heredity for psoriasis, and in one child on dactylitis and first degree heredity for psoriasis.

Fifty of the 321 (15.6%) patients could only be classified as "other arthritis subgroup 1" (Table 3). All 50 patients initially fulfilled criteria for oligoarthritis persistent or oligoarthritis extended, except for one patient with oligoarthritis who dropped out of followup after 6 months. Five patients (5/50) initially also fulfilled criteria for enthesitis-related arthritis. Of 55 classification events, 42 had to be excluded because of psoriasis in a first or second degree relative, 8 because of one or 2 positive RF tests, and 5 because of HLA-B27 associated disease in a first degree relative.

Table 2. Regular ILAR classification in 321 patients. In the right column, classification when heredity for psoriasis in second degree relatives was withdrawn.

ILAR Subgroups	Regular ILAR Classification n	New Classification n
Systemic	13	13
Oligoarthritis, persistent	122	135
Oligoarthritis, extended	17	24
Polyarthritis, RF negative	22	22
Polyarthritis, RF positive	6	6
Psoriatic arthritis	10	9
Enthesitis-related arthritis	12	12
Other arthritis 1, i.e., fits no category	50	28
Other arthritis 2, i.e., fits more than one category	20	22
Polyarthritis, not classified*	39	39
Oligoarthritis, not classified**	10	11
Total	321	321

* Patients with polyarticular disease, but not classified as RF positive or negative because of missing data; ** patients with oligoarticular disease, but not classified as extended or persistent because they dropped out of the followup after 6 months of disease.

The classification results when second degree heredity for psoriasis was excluded from the ILAR classification is shown in Table 2. The group of patients belonging to "other arthritis 1" diminished from 15.6% (50/321) to 8.7% (28/321). Table 4 presents how 23 (23/321) patients changed subgroups. The oligoarthritis extended group increased most.

In 20.6% of our patients (66/321) classified according to the ILAR criteria, there was heredity for psoriasis in a first or second degree relative (or both). The distribution of heredity among ILAR subgroups is shown in Table 5. None of the patients with heredity for psoriasis had a positive RF, but RF was not analyzed in 10 of the patients (10/66, 15%).

Of all 208 patients with a clinical picture of oligoarthritis in our study, 15 had heredity for psoriasis in a first degree relative. When comparing onset type of the oligoarthritis patients (extended or persistent pattern of arthritis, HLA-B27, ANA and uveitis) having first degree heredity for psoriasis versus those with no heredity for psoriasis, the first group was too small to generate reliable results.

DISCUSSION

The proportion in our study of juvenile psoriatic arthritis according to the ILAR criteria, 3.1%, is in accordance with the results of others[7,8,12]. Psoriatic arthritis in children according to the suggested ILAR criteria differs slightly from, for example, definite juvenile psoriatic arthritis based on the Vancouver criteria[10].

Heredity for psoriasis is a highly discriminating variable in the ILAR criteria. Fifteen percent of the patients belonged to "other arthritis 1" subgroup in our study. In the majority of these patients, psoriatic arthritis in a first or second degree relative was the reason. This is in accordance with findings from other studies[7,8,12]. After withdrawal of second degree heredity for psoriasis as an exclusion criterion, 8.7% instead of 15.6% of our patients qualified for "other arthritis 1" subgroup (Tables 1 and 2).

Although 20.6% heredity for psoriasis in first or second degree relatives or both in children with juvenile arthritis might seem high, it should be recalled that we do not know the corresponding figure in healthy children.

The distribution of heredity for psoriasis among subgroups according to the ILAR criteria does not seem to be overrepresented in any subgroup except psoriatic arthritis and "other arthritis 1" subgroup (Table 5). The latter consists of patients with oligoarthritis, persistent or extended, as well as enthesitis-related arthritis, grouped together because second degree heredity for psoriasis is an exclusion criterion. This raises the question of whether heredity for psoriasis is of importance for defining

Table 3. ILAR criteria. Analysis of the 50 patients excluded from 55 possible classification events, consequently classified into "other arthritis 1."

Possible Category	Number of Classification Events	Cause of Exclusion	Number of Classification Events
Oligoarthritis, extended or persistent or not classified as either of them	50	Psoriasis in first degree relative	15
		Psoriasis in second degree relative	22
		One or 2 positive RF	8
		HLA–B27 associated disease, in first or second degree relative	5
Enthesitis-related arthritis	5	Psoriasis in first degree relative	3
		Psoriasis in second degree relative	2

Table 4. Twenty-three (23/321) patients who changed ILAR subgroup when heredity for psoriasis in second degree relatives was withdrawn.

Initial ILAR classification	Number of Patients	New Subgroup
Other arthritis 1 (22 patients)	13	Oligoarthritis, persistent
	7	Oligoarthritis, extended
	1	Oligoarthritis, not classified
	1	Other arthritis 2, i.e., fits more than one category (oligo persistent + enthesitis-related arthritis)
Psoriatic arthrits	1	Other arthritis 2, i.e., fits more than one category (psoriatic arthritis + enthesitis-related arthritis)

subgroups of patients (other than for juvenile psoriatic arthritis).

The purpose for which a classification is designed is an important topic that has been discussed[13], but is worth further emphasis. One of the principal guidelines for the ILAR process is to search for homogeneity within groups. Thus the recent dilemma: if fewer patients fall into the category "other arthritis 1," the result will appear neater but the risk of more diverse groups of patients in the other categories is obvious[14].

We suggest that second degree heredity for psoriasis as an exclusion criterion be withdrawn from the ILAR criteria, not because fewer patients will be classified as "other arthritis 1" but because heredity for psoriasis does not seem specific other than for the category psoriatic arthritis (Table 5). With extended observation time, the pattern of heredity may change as well as the number of patients who develop psoriasis.

None of the 66 patients with heredity for psoriasis was RF positive. Unfortunately the extent to which RF was analyzed was low in our study[15]. In 10 patients (10/66) RF was not analyzed at all, which may have influenced the results.

The family history of psoriasis in the ILAR criteria is restricted to psoriasis of the skin. It seems relevant to keep psoriatic arthritis and psoriatic dermatitis in heredity apart, since research indicates that the propensity to develop psoriasis in the skin or psoriatic arthritis likely overlap without leaving proof for an identical genetic background[16]. Also, psoriasis of the skin relies on more stable diagnostic criteria compared to psoriatic arthritis.

We were unable to compare the onset of disease between oligoarthritis patients with first degree heredity for psoriasis and the remaining patients with oligoarthritis because the former group (15/208) was too small to generate reliable data. Including second degree heredity for psoriasis in the comparison would have increased size of the first group, but would also have made psoriasis heredity a less influential factor. Another important aspect is the short followup (one year at the most) in our study. Continuing to study longitudinal results will reveal the predictive validity of the ILAR criteria.

Table 5. Heredity for psoriasis in 66 (66/321) patients classified according to the ILAR criteria. Heridity comprises first and/or second degree heredity.

ILAR group	Heredity for Psoriasis, n	ILAR Group Total n
Systemic	2	13
Polyarthritis, RF negative	7	22
Polyarthritis, not classified*	11	39
Psoriatic arthritis	8	10
Other arthritis 1, i.e., fits no category	37	50
Other arthritis 2, i.e., fits more than one category	1	20
Remaining ILAR subgroups (oligoarthritis extended, persistent, not classified**, polyarthritis RF positive and enthesitis-related arthritis)	0	167
Total	66	321

* Patients with polyarticular disease, not classified as RF positive or negative because of missing data; ** patients with oligoarticular disease, not classified as extended or persistent because they dropped out of the followup after 6 months of disease.

In recent studies, psoriatic arthritis in adults has been considered to be enthesitis based. Hand and knee disease in psoriatic arthritis is primarily related to enthesitis. This is basically a clinical finding that has recently been supported by typical entheseal abnormalities in psoriatic arthritis revealed by magnetic resonance imaging (MRI)[17,18]. ILAR classification is mainly based on clinical signs, and we are not suggesting that MRI be part of this classification. Considering the new data, however, it seems odd that psoriasis of the skin and enthesitis as clinical variables do not relate at all in ILAR classification. Also, psoriasis in a first or second degree relative is exclusive to enthesitis-related arthritis. As one of the future issues in classification of juvenile arthritis, we suggest that enthesitis-related arthritis should be further evaluated.

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