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Clinical characteristics of juvenile rheumatoid arthritis in Taiwan

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This study aimed to investigate the clinical features of juvenile rheumatoid arthritis among Taiwan children. The medical records of 228 children who had juvenile rheumatoid arthritis treated in the Chang Gung Medical Center in Taiwan from 1978 through 1998 were retrospectively reviewed. A total of 146 boys and 82 girls (M:F ratio, 1.8:1) were included in this study. Clinical and laboratory data of these patients were collected from medical charts. Pauciarticular onset (56%) was the most common type of juvenile rheumatoid arthritis, followed by polyarticular (36%) and systemic (8%) type. The positive rate for rheumatoid factor, human leukocyte antigen B27, and antinuclear antibody were 9.2%, 55.2%, and 16.2%, respectively. Uveitis was observed in 5.7% of patients. Compared with previous reports in other regions and populations, remarkably different features of juvenile rheumatoid arthritis were found in this study, which included a higher prevalence among boys than girls, a high positive rate of human leukocyte antigen B27, and a low rate of uveitis.

Key words: Antinuclear antibody, juvenile rheumatoid arthritis, uveitis

Juvenile rheumatoid arthritis (JRA) is a rheumatic disease most commonly encountered in children [1]. The disease has no known cause; it is not a single but a heterogenous group of diseases [3], and is characterized by chronic synovial inflammation and hyperplasia [2]. Basing on the clinical manifestations during the first 6 months of illness, JRA can be categorized into the following 3 subtypes: polyarticular, pauciarticular, and systemic onset type [4]. Remarkably different features of JRA have been shown in different studies [5-8]. Reports regarding the clinical features of JRA in Taiwanese, however, is lacking. This study sought to determine the clinical characteristics of JRA in a group of Taiwan children.

Materials and Methods

Patients

From 1978 through 1998, 228 children who had experienced JRA were treated at the pediatric rheumatologic clinic or the rheumatologic clinic of the Chang Gung Medical Center, a tertiary care referral hospital in Taiwan. The medical records of these patients were retrospectively reviewed, and information that were collected included the onset type, age at onset, sex, status of rheumatoid factor (RF), status of the human leukocyte antigen B27 (HLA-B27), status of antinuclear antibody (ANA), uveitis, and joint involvement. Age at onset was defined as the age when the first physical sign consistent with the diagnosis of JRA was observed by the patient, his or her parents, or a health worker. Joint involvement was defined as joint swelling or effusion, or the presence of 2 or more of the following findings: limited range of motion, tenderness or pain on motion, or increased warmth of joint, all occurring within the first 6 months of illness. Uveitis was diagnosed by an ophthalmologist, and the patients received regular ophthalmological examinations during the follow-up period.

Inclusion criteria

The American College of Rheumatology terminology and criteria for JRA [4,9] were used as inclusion criteria in this study. Onset type was defined, according to the type of disease manifested in the first 6 months after onset, as: (1) polyarticular onset (≥5 joints involved); (2) pauciarticular onset (≤4 joints involved); and (3) systemic onset (predominance of extraarticular features, eg. fever and rash). Children with infectious arthritis, postinfectious arthritis, juvenile ankylosing spondylitis, or connective tissue disease were excluded.

Laboratory tests

Nephelometry was used in detecting RF; values ≥40 IU/mL were classified as positive. Standard indirect

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Table 1. Distribution of JRA onset type, gender, and mean age at onset

Onset type	No. of patients (%)	Male:female (ratio)	Mean age at onset (yr)
Pauciarticular	127 (56)	97:30 (3.2)	10.6
Polyarticular	82 (36)	38:44 (0.9)	10.7
Systemic	19 (8)	11:8 (1.4)	7.4
Total	228 (100)	146:82 (1.8)	10.4

Abbreviation: JRA = juvenile rheumatoid arthritis

Table 2. Distributions of RF and HLA-B27 positivity in JRA patients

Onset type	Total no. of patients	No. of patients (%)	
		RF+	HLA-B27+
Pauciarticular	127	1 (0.8)	101 (79.5)
Polyarticular	82	20 (24.4)	23 (28.0)
Systemic	19	0	2 (10.5)
Total	228	21 (9.2)	126 (55.2)

Abbreviations: HLA-B27 = human leukocyte antigen B27; JRA = juvenile rheumatoid arthritis; RF = rheumatoid factor

immunofluorescence was used in determining ANA, and Hep-II cells were used as a substrate; titers ≥1:40 were considered positive. Microlymphocytotoxicity assay or direct immunocytometry was used to detect HLA-B27.

Results

The distributions of onset type, sex, and mean age at onset in each subgroup are summarized in Table 1. Pauciarticular onset-JRA (127 cases; 56%) was the most common subgroup, followed by polyarticular (82 cases; 36%), and systemic onset (19 cases; 8%). Boys outnumbered girls by a ratio of 1.8:1. The mean age at onset of this series was 10.4 years.

The age distribution at onset of this series was characterized by a peak incidence among children older than 9 years. A total of 21 (9.2%) children were positive for RF. Among the RF-positive cases, 20 were of the polyarticular subgroup, and 1 was of the systemic (Table 2). Positivity for HLA-B27 was found in 126 (55.2%) cases. The number of HLA-B27-positive JRA patients was high among the pauciarticular subgroup (101 cases; 79.5%) (Table 2).

The positive rate in each JRA type is shown in Table 3. A total of 37 (16.2%) children were ANA positive, and 13 (5.7%) patients have experienced uveitis. Nine of the patients who had uveitis were of the pauciarticular type, 3 were polyarticular, and 1 was systemic. Four of the 13 children with uveitis were ANA positive (Table 3).

Table 4 shows the joint involvement in each of the JRA types. The knee, hip, and ankle were most frequently involved in the pauciarticular type. The knee, ankle, wrist, proximal interphalangeal, and metacarpophalangeal joints were most frequently involved in the polyarticular type. The knee, ankle, wrist, proximal interphalangeal, and distal interphalangeal joints were most frequently involved in the systemic type.

Discussion

In this study, pauciarticular onset-JRA was the most common type in Taiwan children, and its prevalence in boys outnumbered girls by 1.8:1. There is a common perception that pauciarticular JRA is the most frequent onset type, which originated from studies of Caucasian children from North America and Europe [10]. Studies from Asia, however, showed conflicting results, of which pauciarticular, polyarticular, and systemic onset type have all been found to be the most common type [5,6,11-13]. This study conforms with most reports from Asia that boys outnumber girls in the prevalence of JRA [5,6,11,12]. In most Western studies, however, a higher prevalence of JRA was found in girls [7,8,14-16].

The distribution of age at onset varied in previous reports. Tower *et al* [17] and Sullivan *et al* [18] described a bimodal pattern in age distribution, with one peak in children younger than 5 years and another in children aged 10 to 15 years; on the other hand, Schwartz and Andersson-Gäre [19,20] found a distribution peak in

Table 3. Comparison of ANA and uveitis with different onset types of JRA patients

Onset type	Total no. of patients	No. of patients (%)		ANA + Uveitis
		ANA+	Uveitis	
Pauciarticular	127	16 (12.6)	9 (7.1)	3
Polyarticular	82	16 (19.5)	3 (3.7)	1
Systemic	19	5 (26.5)	1 (5.3)	0
Total	228	37 (16.2)	13 (5.7)	4

Abbreviations: ANA = antinuclear antibody; JRA = juvenile rheumatoid arthritis

Table 4. Joints involvement at onset in the three JRA subtypes

Joint	Onset type			Total (n = 228)
	Pauciarticular (n = 127)	Polyarticular (n = 82)	Systemic (n = 19)	
Knee	122	67	10	199
Ankle	47	54	11	112
Hip	58	29	2	89
Wrist	13	54	8	75
PIP	4	52	8	64
MCP	2	48	6	56
Shoulder	12	24	2	48
DIP	2	23	8	33

Abbreviations: DIP = distal interphalangeal; JRA = juvenile rheumatoid arthritis; MCP = metacarpophalangeal; PIP = proximal interphalangeal

young children. In this study, a pubertal peak in distribution similar to previous investigations was found [5,11,15].

A high proportion (55.2%) of HLA-B27 positivity was shown in this study. Similar observations have been reported in studies from Thailand [5], Korea [11], and Norway [8], whereas a low rate of HLA-B27 positivity was found in Japan [6]. Moe and Rygg [8] suggested that the high proportion of HLA-B27 in the JRA population was related to a high prevalence of HLA-B27 in the general population. The low prevalence (2%-6%) of HLA-B27 in Taiwan [21,22], however, suggested that the high proportion of HLA-B27 in this series may have been caused by a high proportion of undifferentiated juvenile spondyloarthropathy [23]. The RF-positive rate (9%) in this study was in accordance with previous reports from Norway [8] and Sweden [20].

In this study, 16% of the cases were ANA positive. This rate is lower than the 30% to 40% reported in the Caucasian populations [24,7], and is higher than the 1% to 6% reported in India [4] and Korea [5]. In reports from the United States [14] and Canada [16], patients of the pauciarticular type had the highest frequency of positive ANA Status. In this study, nevertheless, the highest frequency of ANA positivity (26.5%) was found in the systemic onset type. The reported incidence of uveitis in JRA patients ranged from about 10% to 20% [25-27], but was found in only 13 (5.7%) patients in this study. A low proportion of uveitis was also reported in studies from India [12], Korea [11], and Japan [6]. Despite the general view that there is a strong correlation between uveitis and ANA positivity [28], the frequency of ANA positivity was low in JRA patients who had uveitis in this study.

Ankle and knee were the joints most frequently involved in this series, whereas the small joints of the hands and feet were affected mostly in patients with the polyarticular onset type. These observations are similar to previous studies [5,12,14].

This study is limited by its retrospective nature and hospital-based design. Despite these limitations, this study shows the gross features of JRA among a Taiwanese cohort.

In conclusion, the major characteristics of JRA in Taiwan found in this study included the predominance of pauciarticular onset type, a higher prevalence in boys, pubertal peak in age distribution, high rate of HLA-B27 positivity, low rate of ANA positivity, and low rate of uveitis. This study also suggests the importance of ethnic and geographic location in the clinical features of JRA.

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