

Clinical Observations on Juvenile Rheumatoid Arthritis

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Juvenile rheumatoid arthritis (JRA) is basically the same disease as rheumatoid arthritis in the adult. However juvenile rheumatoid arthritis has many features that differ from rheumatoid arthritis in the adult, and since the onset of the disease occurs before the age of puberty, variable alterations in growth may occur.

In this study, fifty cases of juvenile rheumatoid arthritis treated at Severance Hospital from January 1970 to December 1977 were analysed clinically and the following results were obtained.

1. By classification, the polyarticular type (46%) was most frequent, followed by the pauciarticular type (34%) and systemic type (20%) in order.
2. The most frequent joint affected was the knee (82%) followed by the ankle (60%), hand (22%), wrist (20%), etc.
3. The extra-articular manifestations on admission were high fever (40%), rash (16%), carditis (14%), lymphadenopathy (14%), etc.
4. Laboratory findings on admission showed increased ESR (88%), positive rheumatoid factor (15.5%), positive ANA (16.6%), etc.
5. Clinical symptoms were managed medically and surgically with aspirin, salicylates and steroids, physical therapy, and synovectomy.

Juvenile rheumatoid arthritis is basically the same disease as rheumatoid arthritis in the adult. However juvenile rheumatoid arthritis has many features that differ from rheumatoid arthritis in the adult, and since the onset of the disease occurs before the age of puberty variable alterations in growth may occur.

Rheumatoid arthritis of childhood is often referred to as "Still's disease"; however, it was originally described by Cornil in 1864. Still, in his classic description of 22 cases

of rheumatoid arthritis in children, emphasized the florid form of the disease with fever, lymphadenopathy, and splenomegaly. Since the time of Still many more children with chronic arthritis, which is called Still's disease in England and juvenile rheumatoid arthritis in the United States, have been described.

Rheumatoid disease may begin at any age, the average time of onset being six years of age. It is more common in females (70% of cases). The incidence of juvenile rheumatoid arthritis is about three new cases annually in a general population of 100,000 under 15 years of age. Schaller reported that juvenile

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rheumatoid arthritis is a relatively common chronic disease of childhood in the United States today and it has been estimated that there are one quarter of a million affected children.

MATERIALS AND METHODS

Fifty cases of juvenile rheumatoid arthritis treated at Severance Hospital from January 1970 to December 1977 were analyzed clinically.

1. Sex and types

The sexual incidence was 27 (54%) male and 23 (46%) female patients.

On type of classification, polyarticular type (46%) was most frequent, followed by the pauciarticular type (34%) and the systemic type (20%) in that order (Table 1).

2. Onset of Age

The condition was most common in the 12-15 age group (40%) and showed relatively even distribution in the age group of 3-12. And in the systemic type, it was most common in children under 9 years of age (Table 2).

3. Follow up period

Thirteen cases (26%) were followed for less than 6 months, 10 cases (20%) for 6 months to 1 year and 27 cases (54%) for over 1 year (Table 3).

Table 1. Sex & Types

	Systemic	Polyarticular	Pauciarticular	Total	%
Male	6	15	6	27	54
Female	4	8	11	23	46
Total	10	23	17	50	100
%	20	46	34		100

Table 2. Onset by Age

	Systemic	Polyarticular	Pauciarticular	Total	%
under 3 yrs.	1	1	1	3	6
3 ~ 6 yrs.	2	5	2	9	18
6 ~ 9 yrs.	4	4	1	9	18
9 ~ 12 yrs.	1	3	5	9	18
12 ~ 15 yrs.	2	10	8	20	40
Total	10	23	17	50	100
%	20	46	34		100

Table 3. Follow-up Period

	No.	%
less than 6 mos.	13	26
6 mos. ~ 1 yr.	10	20
1 yr. ~ 3 yrs.	17	34
over 3 yrs.	10	20

Table 4. Predisposing Conditions

	No.	%
U.R.I.	13	26
Infection	3	6
Trauma	2	4

Table 5. Chief Complaints on Admission

	No.	%
Arthralgia	48	96
Fever	16	32
Abdominal pain	4	8
Rash	4	8
Headache	2	4
Sore throat	2	4
Dyspnea	1	2

General characteristics of 50 children with juvenile rheumatoid arthritis were observed clinically with the following observations.

RESULTS

1. Predisposing conditions

Of the 50 cases reviewed, 18 cases were found to have predisposing conditions related to JRA. There were 13 cases of upper respiratory infection (URI), 3 cases of other infections and 2 cases of trauma (Table 4).

2. Chief complaints on admission

On admission, 48 cases (96%) complained arthralgia, 16 cases fever, 4 cases abdominal pain, and 4 cases with rash (Table 5).

3. Extra-articular manifestation

In the systematic type, there was high fever in all cases, in 5 cases (50%) rashes and hepatosplenomegaly, in 3 cases (30%) carditis, and in 2 cases (20%) lymphadenopathy. In the polyarticular type, there were no systemic manifestations except for 9 cases (39.1%) of high fever, and in the pauciarticular type, there were few extra-articular manifestations. How-

Table 6. Extra-articular Manifestations on Admission

	Systemic		Polyarticular		Pauciarticular	
	No.	%	No.	%	No.	%
High fever	10	100	9	39.1	1	5.8
Rash	5	50	1	4.3	3	17.6
Hepatosplenomegaly	5	50	1	4.3	0	0
Lymphadenopathy	2	20	3	13.0	2	11.7
Carditis	3	30	3	13.0	1	5.8
Abdominal pain	4	40	2	8.6	0	0
Pleuritis	0	0	2	8.6	0	0
Rheumatoid nodule	0	0	2	8.6	2	11.7

Table 7. Frequency of Involved Joints

	Systemic	Polyarticular	Pauciarticular	Total	%
Knee joint	8	21	12	41	82
Ankle joint	6	18	6	30	60
Wrist joint	3	6	1	10	20
Elbow joint	1	7	0	8	16
Hand joint	5	6	0	11	22
Hip joint	0	4	2	6	12
Cervical spine	0	1	0	1	2
Others	0	5	0	5	10

ever, in 2 cases, rheumatoid nodules were palpated in the elbow area in polyarticular and pauciarticular type respectively (Table 6).

4. Frequency of involved joints

The most frequent joint affected was the knee (82%) followed by ankle (60%), hand (22%), wrist (20%), elbow, hip, cervical spine and others. The knee and ankle joints especially, were affected in the pauciarticular type (Table 7).

5. Radiological findings

Radiological findings revealed 13 cases (26%) of soft tissue swelling, 5 cases (10%) of osteoporosis, 3 cases (6%) of joint space narrowing and only 1 case (2%) of ankylosis (Table 8).

6. Laboratory findings on admission

From the laboratory findings, 15 cases (30%) of patients were found to have anemia, 18 cases (36%) leukocytosis and 44 cases (88%) increased ESR which was the most significant laboratory finding in the JRA study. Also, 26 cases (52%) of increased ASO titer and 22 cases (44%) of positive CRP were found. Of the 45 cases studied, 7 (15.5%) were found to have a positive RA factor, 2 (16.6%) out of 12 cases studied were positive for antinuclear antibody (ANA)

Table 8. Radiological Findings

	No.	%
Soft tissue swelling	13	26
Osteoporosis	5	10
Joint space narrowing	3	6
Ankylosis	1	2

study, and one case was associated with iridocyclitis (Table 9).

7. Duration of illness prior to admission

Eleven cases (22%) were of less than 3 months duration and most of them were patients of the systemic type. Thirteen cases (26%) were of 3-6 months and 12 cases (24%) were of over 3 years duration (Table 10).

8. Hospital periods

The admission period varied from 2 to 49 days, and the average was 11 days.

9. Treatment

Twenty-seven cases (54%) were treated with aspirin only, 13 cases (26%) were treated with aspirin and steroids and 31 cases (62%) with antibiotics and other drugs.

In addition to medical treatment, 12 cases (24%) were treated with physical therapy and

Table 9. Laboratory Findings on Admission

	Systemic(10)		Polyarticular(23)		Pauciarticular(17)		Total	
	No.	%	No.	%	No.	%	No.	%
Anemia	4	40	9	39.1	2	11.7	15	30
Leukocytosis	7	70	7	30.4	4	23.4	18	36
Increased E.S.R.	9	90	20	86.9	15	88.2	44	88
Increased A.S.O.	4	40	14	60.8	8	47.0	26	52
Positive C.R.P.	6	60	9	39.1	7	41.1	22	44
Positive R.A.(45)	0	0	5	21.7	2	11.7	7	15.5
A.N.A. (12)	0	0	1	4.3	1	5.8	2	16.6

Table 10. Duration Prior to Admission

	No.	%
less than 3 mos.	11	22
3 mos. ~ 6 mos.	13	26
6 mos. ~ 1 yr.	6	12
1 yr. ~ 3 yrs.	8	16
over 3 yrs.	12	24

8 cases (16%) were treated with traction and brace. Synovectomy was performed in only one case (Table 11).

10. Functional class

During the follow-up period, the results were analysed according to the functional class criteria of the American Rheumatism Association (Table 12).

No case belonged to class IV.

In the systemic type, one case was class III and 3 cases were class II.

In the polyarticular type, 3 cases were class III and 4 cases were class II.

In the pauciarticular type, one case was class III and 4 cases were class II.

Of the total 50 cases 34 were class I (Table 13).

Table 11. Treatment

	No.	%
Salicylate	27	54
Salicylate & steroid	13	26
Salicylate & intra-articular steroid	4	8
Salicylate & steroid & intra-articular steroid	3	6
Brufen	2	4
Salicylate & chloroquine	1	2
Antibiotics & drugs	31	62
Physical therapy	12	24
Traction	4	8
Brace or splint	4	8
Synovectomy	1	2

Table 12. Functional Class

- Class I: Complete function (ability for all usual activities without handicap)
- Class II: Adequate function (adequate for normal activities despite handicap, discomfort or limited motion at one or more joints)
- Class III: Limited function (significant limitation in the duties of usual occupation and selfcare)
- Class IV: Incapacitated (confined to bed or wheel chair with little or no selfcare)

Table 13. Results of Functional Class

	Systemic	Polyarticular	Pauciarticular	Total
Class I	6	16	12	34
Class II	3	4	4	11
Class III	1	3	1	5
Class IV	0	0	0	0
Total	10	23	17	50

DISCUSSION

Many authors, including McDuffie, (1971) have claimed that the etiology of JRA was according to the autoimmune theory, and that the rheumatoid factor was 19s IgM reacting with the antibody, 7s IgG. Tachdjian (1972) believed that the inflammation resulted from deposition of this reumatoid factors within the joint, which caused release of lysosomal enzymes, the accelerated release of which initiated and proliferated damage to the joint. However, Edstrom (1958), Saïranen (1962), Laaksonen (1966), and Baum and Fink (1968) reported the genetic theory of the etiology of JRA. Tachdjian (1972) and Williams (1968) reported the direct infection theory by mycoplasma.

Rheumatoid arthritis in children varies greatly in its clinical manifestations, type of onset, course, and prognosis. Schaller (1974), in her observation of 124 cases reported that 25% were of the systemic type, 40% of the polyarticular type and 35% of the pauciarticular type. Calabro (1974) reported 20% of his cases were of the systemic type, 50% of the polyarticular type and 30% of the pauciarticular type. In our study, we observed a similar incidence to theirs. According to Tachdjian (1972), rheumatoid disease may begin at any age, the average time of onset being six years of age. It starts most frequently in the one to four-age

group, with another rise in incidence at puberty (9 to 14-year age group). Calabro (1974), in his study of JRA, reported that the average age at onset of this disease was 4.6 years in systemic type, 7.4 years in the polyarticular type and 7.3 years in the pauciarticular type. In our study, most of the patients of systemic type developed the disease under the age of nine.

As for sex ratio, Schlesinger (1961) reported that 40 cases were male and 60 cases female; Sullivan (1974), 87 cases male and 213 cases female; and Schaller (1974), in 124 cases, male patients were more prevalent than female in the systemic type, but females were much more frequent than males in the polyarticular and pauciarticular types. Female patients were more involved than males in total JRA cases and Tachdjian (1972) reported that the condition was more common in girls, the female to male ratio being 7:3. In our study, JRA was most common in the age group 12-15 years, there was no significant sexual difference and the polyarticular type was the most frequent.

Pathologically, JRA is characterized by a non-suppurative inflammation and the disease, as a rule, first manifests with edema and hypervascularity, allowing migration of the leukocytes into the synovial tissues and joint fluid. According to Tachdjian (1972), with the progression of inflammation, the synovial cells proliferate and the synovium becomes thickened, forming nodules and villi that project

onto the joint surface and forms a pannus. As the pannus spreads onto the articular surface, the subchondral bone undergoes destruction from both sides and joint ankylosis, accelerated epiphyseal growth or premature fusion of epiphyseal growth plate may ensue.

Clinically, Calabro (1974) reported that a high fever may antedate detectable arthritis by weeks, months, or even years, so careful observation is needed. Also a rash is usually widespread in 80% of patients, occurring on the trunk, face, and extremities as well as on the soles and palms. This rash is most florid in areas where the skin has been rubbed or subjected to mild trauma such as the light pressure of clothing. This manifestation is known as the Koebner phenomenon and may be useful diagnostically when parents report a rash that is not evident at the time the child is being examined. In addition, 85% of patients were found to have hepatosplenomegaly and leukocytosis.

The important disorders for differential diagnosis are rheumatic fever, systemic lupus erythematosus, Henoch-Schonlein purpura, and leukemia. Calabro (1974) pointed out several other features of JRA to help rule out rheumatic fever. The followings are the most important: (1) onset before 4 years of age, (2) cervical involvement (3) poor mucin on synovial fluid analysis, (4) generalized lymphadenopathy, (5) hepatosplenomegaly in the absence of cardiac failure, and (6) arthritis lasting more than 12 weeks. He pointed out that in the polyarticular type, systemic manifestations occurred less frequently than in the systemic type and the fever was low grade.

In the polyarticular type, the arthritis is confined to the large joints and is asymmetric or migratory. It may be confused with other rheumatic disorders, particularly rheumatic fever. Schaller (1974) said that ulnar deviation at the

metacarpophalangeal joints occurs rarely in JRA; indeed radial drift is sometimes present and rupture of finger tendons is uncommon in children. He said that cervical spine involvement with stiffness of the neck occurred in about one half of all patients: subluxation of C1 to C2 occurred occasionally, but secondary cord problems were rare. Schaller (1974), Calabro (1974), and Tachdjian (1972) reported that the most involved joints were the knee and ankle, but that, in addition, the hip, elbow, hand and subtalar joints were often involved. In our study, the most frequently affected joint was the knee followed by the ankle.

In the pauciarticular type, systemic manifestations are rare. According to Barry (1975), Calabro (1974), and Schaller (1974), the most serious manifestation of the pauciarticular type is iridocyclitis, which may even occur in from one fourth to one third of patients at unpredictable intervals during the first ten years of the disease, so regular slit lamp examination to detect the first signs of iridocyclitis should be taken for prevention of blindness. Schaller (1974) reported that tests for antinuclear antibodies were positive in 90% of children with iridocyclitis of JRA. In our study, 2 cases (16.6%) of 12 studied were positive for ANA.

There was no pathognomonic laboratory test for JRA. As noted previously, anemia may be present and leukocytosis may be pronounced. Elevation of the sedimentation rate is generally associated with active inflammation, but sedimentation rates are occasionally normal in children with active JRA, particularly in those with pauciarticular disease. Calabro (1974) and Schaller (1974) reported that rheumatoid factors, which are antibodies reactive with IgG immunoglobulin, were found in 85% of adults with rheumatoid arthritis, but positive in only 10-25% of children with JRA. Positive tests were found primarily in the polyarticular

type among children 12-16 years of age. Antinuclear antibodies occur in 10-30% of children with polyarticular and pauciarticular JRA, but rarely in patients with systemic JRA. They occur most frequently in girls and rarely before 6 years of age, but Miller (1966) claimed that this was positive most frequently in boys. In our study, 44 cases (88%) showed increased ESR, and 7 cases (15.5%) of 45 cases studied were positive for RA factor. Calabro (1974) reported that prolonged and moderately elevated ASO titers occurred in about 30% of patients with JRA, but these titers appeared to be non-specific. Generally, persistently elevated levels of IgG, IgA, and IgM are associated with an increased incidence of hip involvement and, poor functional status and serum electrophoresis may reveal low albumin and elevated beta and gamma globulins.

The prognosis for children with JRA is favorable. According to Calabro (1974), 60 cases out of 100 patients were in functional class I and II, and only 11 patients were in the unfavorable functional class of III and IV. Schaller (1974), in 124 cases studied, said he could be sure that only 13% of patients had severe joint disease; 25% of systemic onset patients, 17% of polyarticular onset patients, and no pauciarticular patients had severe joint disease. In our study, 16 cases were class II or III, and 34 cases were class I.

In the management of the rheumatoid child, it is imperative to employ a multidisciplinary approach. During the acute inflammatory stage, local and general rest are necessary, as well as a well balanced, nutritious diet with an ample supply of proteins, minerals and vitamins. Aspirin is the most useful and generally effective anti-inflammatory agent in the treatment of rheumatoid arthritis. According to Calabro (1974) and Tachdjian (1972), to achieve a therapeutic response,

salicylate blood levels of 20 to 30 mg/100 ml should be maintained by administration of four to six daily doses, totaling 90 to 130 mg/kg. Early signs of chronic salicylate intoxication are easily overlooked and parents are instructed to watch for lethargy and episodic hyperpnea, which are changes especially important in the child who is too young to complain of tinnitus. Calabro (1974) administered adrenosteroids to patients with heart failure caused by myocarditis, as well as to patients with pericarditis, vasculitis, and protracted iridocyclitis.

Other medical drugs are gold salts of chrysotherapy, chloroquine, phenylbutazone, ACTH, azathioprine, cyclophosphamide, but according to Zutshi (1971) these drugs are not used routinely because of their frequent toxic effects. In addition to medicine, physical therapy and braces are used to treat the child with JRA. Eyring (1974) listed the general principles of use of braces; 1) the external support should be as simple to use as possible 2) the less external supports are used the better 3) inexpensiveness of the external support. Other considerations include: the age of the patient, the type of disease, extent of disease, functional status, and associated problems.

In operative treatment, there are soft tissue release operations and synovectomy in the early stages, and arthroplasty, osteotomy and arthrodesis in later stages. The soft tissue release operation was introduced to us by Jakubowski (1967). He performed a release of contracted soft tissues which decreased the intra-articular pressure, increased the range of joint motion and relieved pain. It was more effective in operations on large joints such as the hip or knee. Granberry and Brewer (1974) believe that an absolute diagnosis is necessary before contemplating surgery, and they would wait six months or more after onset of the disease before considering synovectomy. Bianco and Peterson

(1971) pointed out the indications for synovectomy for children with JRA. : 1) As therapeutic synovectomy, when there are acute synovitis with destructive changes by X-ray 2) In spite of adequate conservative treatment, when there is acute synovitis with marked decrease of range of joint motion. 3) As preventive synovectomy, when there is acute synovitis, although no destructive changes on X-ray or no decreased range of joint motion is found. Issacson (1974) said that, regardless of the pain situation in children, to beware and not operate on the dry type of progressive arthritis because the amount of stiffness that resulted was tantamount to arthrodesis of these joints. We managed most of our patients by means of drugs and physical therapy with good results and performed one case of synovectomy in a case of pauciarticular type involving knee joint and obtained a good results.

CONCLUSION

Fifty cases of JRA treated at the Severance Hospital from January 1970 to December 1977 were clinically analysed and the following results were obtained.

On type classification, the polyarticular type was most frequent followed by the pauciarticular type, and the systemic type in that order. The most frequently affected joints were the knee and ankle. The extra-articular manifestations on admission were high fever, rash, carditis and lymphadenitis.

Laboratory findings on admission showed increased ESR, which was the most significant test for this disease, positive rheumatoid factor and positive ANA which was an important test to diagnose iridocyclitis and prevent blindness in polyarticular and pauciarticular type cases of JRA.

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