

Frequency of Abnormal Hand and Wrist Radiographs at Time of Diagnosis of Polyarticular Juvenile Rheumatoid Arthritis

TOM MASON, ANN M. REED, AUDREY M. NELSON, KRISTEN B. THOMAS, ALICE PATTON, ALAN D. HOFFMAN, SARA ACHENBACH, and WILLIAM M. O'FALLON

ABSTRACT. Objective. To determine the frequency of radiographic abnormalities in hand/wrist radiographs of children with newly diagnosed polyarticular juvenile rheumatoid arthritis (polyJRA) because radiographs of small joints are an important tool in assessing outcomes in RA and there are clinical similarities between RA and polyJRA.

Methods. A medical record review was performed to identify cases of polyJRA seen at Mayo Clinic from January 1, 1994, to December 31, 2001. Hand/wrist radiographs, obtained at the time of diagnosis, were reviewed by 3 radiologists with attention to periarticular osteopenia, joint space narrowing (JSN), or erosion. At least 2 radiologists had to independently identify abnormal findings on the same radiograph. The relative carpal length (RCL), judged by Poznanski's method, was also determined.

Results. From the review of 159 medical records, 60 cases of newly diagnosed polyJRA were identified. Twenty-five of these had hand/wrist radiographs at diagnosis; 18 sets were available for this study. Of those, 2/3 were female, 6% (1/18) had subcutaneous nodules, 7% (1/14) had elevated levels of serum rheumatoid factor, and 44% (7/16) had elevated serum levels of antinuclear antibodies. Median age at diagnosis was 10.2 years, median duration of hand/wrist symptoms at diagnosis was 10 months, and median number of joints with either swelling, pain on range of motion (ROM), or limited ROM was 14.5. Sixty-one percent of radiographs taken at the time of diagnosis of polyJRA were abnormal. While 44% had periarticular osteopenia, 28% had either erosions or JSN. Six (33%) had RCL > 2 SD below the mean for age. Five (83%) of those with RCL, > 2 SD below the mean for age, had periarticular osteopenia, JSN, or erosion.

Conclusion. We conclude the frequency of abnormal hand/wrist radiographs is very high very early in the course of polyJRA. More studies are needed to determine to what extent these radiographic abnormalities correlate with clinical outcomes. (J Rheumatol 2002;29:2214-8)

Key Indexing Terms:

JUVENILE

ARTHRITIS

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Juvenile rheumatoid arthritis (JRA) is a common chronic illness of childhood with an incidence rate of roughly 1 per 10,000 children per year and a prevalence rate of roughly 1 per 1,000 children¹. There are 3 distinct subtypes based on the clinical presentation of the illness². About 10% of children present with fevers, rashes, and an inflammatory arthritis and are labeled as systemic onset JRA. The most common subset of JRA is pauciarticular JRA, which is characterized by 4 or fewer synovial joints being inflamed in the

absence of systemic features. Polyarticular JRA (polyJRA) is defined by the presence of arthritis in 5 or more joints with the absence of systemic features. The diagnosis of these illnesses is based on the 1977 American Rheumatism Association criteria³.

Assessing outcomes of therapy is a very important part of managing children with JRA. In adults with RA, a number of outcome assessments have been developed, some of which are constructs of clinical and laboratory assessments including global assessments by patients and physicians, functional assessments, joint counts, and measurements of acute phase reactants⁴. Another important evaluation in assessing outcomes in adults with RA is serial study of plain radiographs. Studies have shown that abnormalities of radiographs of the hands and wrists correlate well with other clinical outcome measures for patients with RA^{5,6}.

While there are a number of scoring systems available to assess these radiographic variables in adults with RA, no such scoring system exists to assess similar changes in children with JRA. A potential reason for this deficiency is that

From the Division of Rheumatology, Departments of Radiology and Health Sciences Research, Mayo Clinic, Rochester, Minnesota, USA.

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T. Mason, MD, Assistant Professor of Medicine and Pediatrics; A.M. Reed, MD, Associate Professor of Pediatrics; A.M. Nelson, MD, Professor of Medicine; K.B. Thomas, MD, Instructor in Radiology; A. Patton, MD, Associate Professor of Radiology; A.D. Hoffman, MD, Associate Professor of Radiology; S. Achenbach, MS; W.M. O'Fallon, PhD, Professor of Biostatistics.

Address reprint requests to Dr. T. Mason, Division of Rheumatology, Mayo Clinic, 200 First St. SW, Rochester, MN 55905, USA.

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JRA has 3 subtypes, each with differing distributions of articular involvement. Another issue is that osseous maturation in children evolves over a number of years, thus younger children do not have comparable radiographic appearance of diarthrodial joints if they are at different stages in development. This is particularly problematic in the wrist, a joint very frequently involved in children with polyJRA.

An attempt to quantify the relative amount of articular cartilage in the wrists of children called relative carpal length (RCL) has been presented by Poznanski, *et al*⁷. This involves measuring the distance between the base of the 3rd metacarpal bone and the midpoint of the distal radial growth plate (RM). The shorter this distance is relative to the length of the 2nd metacarpal bone, the higher the likelihood of further radiographic progression.

The general variables in assessing radiographic damage in RA include osteopenia, joint space narrowing, and the presence of cortical erosion⁸. The presence of erosions in patients with RA suggests a high likelihood of joint damage and poor clinical outcomes⁹. PolyJRA shares many clinical features with RA, including frequent involvement of the hands and wrists. As with RA, the natural history of the articular involvement of polyJRA is progressive and potentially destructive.

The frequency of these radiographic findings (periarticular osteopenia, JSN, and erosions) in children with polyJRA is unknown. These findings are associated with poor clinical outcomes in adults with RA, but the outcomes are unknown in children with polyJRA. In patients with RA, abnormalities on hand/wrist radiographs performed at diagnosis were highly predictive of further progression¹⁰. Because radiographic abnormalities at the time of diagnosis in children with polyJRA might have similar prognostic utility, we reviewed medical records and hand/wrist radiographs of children with polyJRA to assess the frequency of these radiographic findings.

MATERIALS AND METHODS

Medical record review. The indexed diagnoses from all medical records of patients seen at Mayo Clinic Rochester from January 1, 1994, to December 31, 2001, were reviewed. The diagnoses of JRA, juvenile arthritis, or juvenile chronic arthritis were identified in 164 medical records. For 5, no consent was given for medical record review. Of 159 medical records reviewed, 62 were not seen by a Mayo Clinic rheumatologist within 12 months of the onset of symptoms attributable to polyJRA (so-called "second opinion" evaluations), and were excluded from the study. The remaining 97 charts were carefully reviewed to confirm the diagnosis of JRA by 1977 American Rheumatology Association criteria³. Eight of these had the diagnosis of RA made after 16 years of age, 7 more were unlikely to have had JRA (3 with other connective tissue diseases, one with leukemia, 2 with genetic syndromes, and one with avascular necrosis). Another 22 had JRA, but the wrong subtype (7 with pauciarticular JRA, 7 with systemic onset JRA, and 8 with extended pauciarticular JRA). The principal investigator reviewed all available medical records, including the remaining 60 patients, and data extracted from these medical records were recorded on a data collection sheet.

Radiographic methods. The 3 participating radiologists were presented radiographs of the hands/wrists and were asked to interpret them and record their results on a preprepared data collection form, commenting on the presence of soft tissue swelling, periarticular osteopenia, joint space narrowing (JSN), or pericortical erosions. All are pediatric radiologists and one had advanced training in skeletal radiology. The radiologists were blinded to any information about the subjects, except for the child's sex, date of birth, and the date the radiograph was performed. Each radiologist read the radiographs independently. For this study, 2 of the 3 radiologists had to agree on the interpretation of a finding (osteopenia, JSN, or erosion) for it to be counted as an abnormality.

In addition, one radiologist familiar with Poznanski's technique⁷ performed the measurements of the radiocarpal length (RM) and length of the second metacarpal (M2) in mm. These measurements were also recorded on a preprepared data collection sheet and were plotted on the curve derived by Poznanski, *et al* to assess RCL for age. RCL was recorded as the number of standard deviations (SD) below the mean for age from this reference. For this study, an RCL > 2 SD below the mean for age was defined as shortened.

Data analysis. Demographic characteristics and variables of interest were described using appropriate summary statistics. Continuous variables were compared between 2 groups using the Wilcoxon rank-sum test. Chi-square tests were done to compare discrete variables between the 2 groups.

RESULTS

All of the 60 children with polyJRA were Caucasian, and 75% were female. Median age at the time of diagnosis of polyJRA was 9.9 years, and the median duration of hand/wrist symptoms at the time of diagnosis was 4 months. The median number of involved joints [decreased range of motion (ROM), painful ROM, or swelling] at the time of diagnosis was 16. At the time of diagnosis, 4 of 90 (7%) had subcutaneous nodules, 11 of 48 (23%) had an elevated serum rheumatoid factor (RF), and 22 of 52 (42%) had serum antinuclear antibodies (ANA) in an elevated titer.

Of these, 35 did not have a baseline radiograph obtained at the time of diagnosis. The remaining 25 cases had hand/wrist radiographs done at the time of diagnosis of polyJRA. The 25 with baseline hand/wrist radiographs had a longer duration of hand/wrist symptoms at diagnosis compared to those without baseline hand/wrist radiographs (7.0 ± 4.2 vs 4.4 ± 3.2 months; $p = 0.02$). There were no statistically significant differences between those with baseline radiographs and those without based on race, sex, age at diagnosis of polyJRA, number of involved joints, presence of nodules, RF, or ANA. Of the 25 cases with baseline radiographs, 18 sets of radiographs were available for this study (72%).

All of the 18 children (who had hand/wrist radiographs) in this study were Caucasian; two-thirds were female. The median age at diagnosis was 10.2 years, the median duration of hand/wrist symptoms attributable to polyJRA was 10 months, and the median number of involved joints was 14.5. One child had subcutaneous nodules. Serum RF was available on 14, one of which (7%) was positive. ANA status was available on 16 patients, of which 7 (44%) had serum elevated levels.

The results of the radiologists' review of the radiographs

are described in Table 1. Eight (44%) had periarticular osteopenia at the time of diagnosis. Three (17%) had JSN and 3 (17%) had erosions at the time of diagnosis. Only 7 (39%) hand/wrist radiographs taken at the time of diagnosis of polyJRA were judged to have no abnormality.

A comparison of subjects with normal and abnormal hand/wrist radiographs is shown in Table 2. Those that had abnormal radiographs were less likely to be female (64 vs 71%), a little older (median age at diagnosis 10.7 vs 9.2 years), had similar duration of hand/wrist symptoms at diagnosis, a slightly lower number of involved joints at diagnosis (median 14 vs 15), and were less likely to be ANA positive (33 vs 57%). As expected, the one patient with a subcutaneous nodule and positive serum RF had abnormal hand/wrist radiographs.

A comparison of subjects with and without erosions is shown in Table 3. Those with erosions were as likely to be female, a little older (median age at diagnosis 11.7 vs 9.4 years), had slightly longer duration of hand/wrist symptoms at diagnosis (median 11 vs 10 months), had slightly fewer involved joints at the time of diagnosis (median 14 vs 15),

and were less likely to be ANA positive (0 vs 50%). Subcutaneous nodules and RF positivity were associated with a higher likelihood of erosions.

A comparison of subjects based on shortened RCL is shown in Table 4. Six (33%) had shortened RCL. Those with shortened RCL were less likely to be female. They were older (median age at diagnosis 12.6 vs 9.3 years), had longer duration of hand/wrist symptoms at diagnosis (median 10.5 vs 5.5 months), had fewer involved joints at the time of diagnosis (median 14 vs 17), and were slightly more likely to be ANA positive (50 vs 42%). The patient with nodules and positive RF did not have a shortened RCL. Of the 5 radiographs with either JSN or erosions, 3 had shortened RCL (the other 2 had relative carpal length 1–2 SD below the mean for age). Five of the 6 radiographs with shortened RCL were read as abnormal.

DISCUSSION

This is the first study to systematically evaluate the frequency of abnormal hand/wrist radiographs at the time of diagnosis of polyJRA. The utility of these types of radio-

Table 1. Radiologists' interpretation of hand/wrist radiographs of children with polyJRA at diagnosis.

Subject	Periarticular Osteopenia (Rd1/Rd2/Rd3)	Joint Space Narrowing (Rd1/Rd2/Rd3)	Erosions (Rd1/Rd2/Rd3)	Normal Radiographs
1	Yes/Yes/Yes	No/No/No	No/No/No	No
2	Yes/Yes/Yes	Yes/Yes/Yes	Yes/Yes/Yes	No
3	No/No/No	No/No/No	No/No/No	Yes
4	Yes/No/Yes	No/Yes/No	No/No/No	No
5	No/No/No	No/No/No	No/No/No	Yes
6	Yes/No/Yes	No/No/No	No/Yes/Yes	No
7	No/No/No	No/No/No	No/No/No	Yes
8	No/No/No	Yes/Yes/No	No/No/No	No
9	Yes/No/Yes	No/No/No	Yes/No/No	No
10	No/No/No	Yes/Yes/No	No/Yes/No	No
11	No/No/Yes	No/No/No	No/Yes/No	Yes
12	No/No/No	No/No/Yes	No/Yes/Yes	No
13	No/No/Yes	No/No/No	No/Yes/No	Yes
14	Yes/No/Yes	No/No/No	No/No/No	No
15	No/No/Yes	No/No/No	No/No/No	Yes
16	Yes/No/Yes	No/No/No	No/No/No	No
17	No/No/Yes	No/No/No	No/No/No	Yes
18	Yes/Yes/Yes	No/Yes/No	No/No/No	No
No. (%) of cohort	8 (44)	3 (17)	3 (17)	7 (39)

Rd1: radiologist #1; Rd2: radiologist #2; Rd3: radiologist #3. Number (%) of cohort = number (%) of the cohort who had this radiographic abnormality.

Table 2. Comparison of clinical features of children with polyarticular JRA with normal versus abnormal hand/wrist radiographs.

Radiographs (n)	Female, %	Median Age at Diagnosis, yrs	Median Months of Symptoms at Diagnosis	Median No. of Involved Joints at Diagnosis	Nodules, %	RF Positive, %	ANA Positive, n (%)
Normal (7)	71	9.2	10	15	0	0	4/7 (57)
Abnormal (11)	64	10.7	10	14	9	11	3/9 (33)

Table 3. Comparison of clinical features of children with polyarticular JRA with erosions on hand/wrist radiographs versus those without.

	Female, %	Median Age at Diagnosis, yrs	Median Months of Symptoms at Diagnosis	Median No. of Involved Joints at Diagnosis	Nodules, %	RF Positive, %	ANA Positive, n (%)
No erosions, n = 15	67	9.4	10	15	0	0	7/14 (50)
Erosions present, n = 3	67	11.7	11	14	33	1/2 (50)	0/2 (0)

Table 4. Features of children with polyJRA with shortened RCL for age.

RCL	Female, %	Median Age at Diagnosis, yrs	Median Months of Symptoms at Diagnosis	Median No. of Involved Joints at Diagnosis	Nodules, %	RF Positive, %	ANA Positive, n (%)
< 2 SD below mean for age, n = 12	92	9.3	5.5	17	8	10	5/12 (42)
≥ 2 SD below mean for age, n = 6	17	12.6	10.5	14	0	0	2/4 (50)

RCL: relative carpal length (Poznanski⁷).

graphic studies is well described in RA. Thirty percent to 50% of patients with RA will have erosions within 3 years of their diagnosis¹¹. Recent community based cohort studies suggest that early in the course of the disease this rate may be less, but that some patients with RA will get erosions several years after disease onset¹². RA patients with abnormal radiographs, particularly those with erosions, have worse clinical outcomes¹⁰.

The ratio of females, subcutaneous nodules, and RF positivity in our cohort of polyJRA is similar to other reports². Duration of joint symptoms at the time of diagnosis and number of involved joints at the time of diagnosis are not frequently reported in the literature. The mean age at diagnosis of polyJRA in this cohort (9.9 ± 4.2 yrs) is higher than our population based cohort (about 6 ± 4 yrs)¹.

The findings from this study are not consistent with the view that JSN and erosions generally do not occur with JRA before 2 years of arthritis, even in children with polyarthritis². In fact, our study would suggest that these types of radiographic findings are common at the time of diagnosis of polyJRA. Several studies have suggested that children with polyJRA do not have destructive changes such as JSN or erosions early in their illness, except for RF positive polyJRA^{13,14}. Children with RF positive polyJRA seem to have a particularly aggressive illness, with greater than 90% having erosions within 5 years of diagnosis¹⁵. Only one member of this cohort was RF positive.

A retrospective study of radiographs of affected joints in children with systemic onset JRA revealed that 50% developed JSN or erosion within 2 years of diagnosis¹⁶. In another study on a cohort of children with systemic onset

JRA, risk factors for joint destruction were found 2 years after diagnosis¹⁷. Those who were more likely to have these destructive radiographic changes were more likely to have had serositis, hepatosplenomegaly, and lower serum albumin levels at initial evaluation. In this same study, persistence of systemic symptoms, polyarthritis, and a number of laboratory markers suggesting persistent inflammation 6 months after diagnosis were also strong predictors of destructive radiographic findings.

Our study is substantially different than those, some of which were reported more than 20 years ago. In those studies, radiographs were performed on any affected joints, not just hand/wrist joints. Their treatment of polyJRA was very likely to affect the radiographic findings in those studies, but the most important difference between those studies and ours is that our cohort's radiographs were performed at the time of diagnosis. Our data suggest that these radiographic abnormalities are frequent and occur much earlier than previously thought. The observation that these radiographic changes were at the time of diagnosis highlights the need for timely diagnosis of JRA. A further delay in diagnosis would allow for more potential progression. Perhaps serial study of these simple radiographs might correlate with clinical outcomes and thus be helpful in guiding therapies for polyJRA in a fashion similar to RA.

The limits of studies based on data collection from chart review are clear. No subject of this study was examined to verify the findings documented in the medical records. These data are limited by the degree to which the clinicians evaluating these children documented their findings. We could not accurately assess whether the children with more

severe polyJRA might have been more likely to have had hand/wrist radiographs, since the clinical data were not prospectively collected. An attempt was made to look for potential risk factors for abnormal initial radiograph. The small number of subjects in this study precluded this.

No previous study of radiographs from children with JRA has utilized more than one radiologist. Agreement between the radiologists was not uniformly consistent between radiographic variables (periarticular osteopenia, JSN, and erosions). There was more agreement in the assessment of JSN than periarticular osteopenia or erosions. The radiologists had no other special preparation with regard to this study. Each radiologist reviewed all of the radiographs in one session with no additional clinical input. The variation in their interpretations points to the need for a standardized method to systematically evaluate hand/wrist radiographs in children with polyJRA.

We also compared the Poznanski technique assessing RCL to variables used to assess damage in adults with RA in children with newly diagnosed polyJRA. There was no statistically significant correlation between the 2 techniques, but significant abnormalities in both techniques were observed in the same radiographs of several subjects.

This study will serve as pilot data for a potential prospective study to collect clinical and serial radiographic data from children with polyarticular JRA to see if radiographic assessments, such as the findings of erosions, correlate with poorer clinical outcomes (and if so, to what degree) in these children. Findings from that study could result in the development of a scoring system for hand/wrist radiographs similar to those used for RA.

In our review of hand/wrist radiographs from 18 cases of polyJRA, more than half were felt to be abnormal at the time of diagnosis by a panel of 3 radiologists. Almost 45% had periarticular osteopenia, 17% had JSN, and 17% had at least one erosion. One-third of this cohort had RCL > 2 SD below the mean for age. These data suggest that radiographic abnormalities in polyJRA are common, even at the time of diagnosis.

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