Unilateral destructive wrist synovitis in juvenile idiopathic arthritis

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Abstract

Objective

To describe the clinical and radiographic features of a group of juvenile idiopathic arthritis (JIA) patients who developed unilateral destructive wrist synovitis.

Methods

All wrist radiographs performed yearly between 1986 and 2002 in JIA patients who had wrist involvement were retrospectively reviewed to identify patients who had unilateral erosive wrist synovitis, defined as a difference of at least –3 units in the Poznanski score between the affected wrist and the unaffected wrist, with the Poznanski score in the unaffected wrist being > –2 units throughout the follow-up period. Clinical and radiographic data obtained during follow-up were recorded for all patients.

Results

Of a total of 250 patients for whom we had approximately 900 wrist radiographs, 6 patients were found to have unilateral erosive wrist synovitis. The JIA onset subtype was oligoarticular in 5 patients and polyarticular in 1 patient and the disease duration from presentation to the last follow-up visit ranged from 2 to 16 years. The arthritis course was polyarticular in all patients. Five patients had positive antinuclear antibodies (ANA) and 1 had positive rheumatoid factor (RF). At the last follow-up visit, all patients had some impairment of wrist function and 2 patients had wrist subluxation. There was a marked radiographic damage in all affected wrist, with the Poznanski ranging from –8.0 to –8.50 units in 3 patients and being –5.5, –3.1 and –2.4 units, respectively, in 3 patients. The severity of radiographic damage in the ANA-positive patients with the longest disease duration was comparable to that observed in the RF-positive patient.

Conclusion

Unilateral erosive wrist synovitis seems to be uncommon in JIA. Patients with unilateral wrist synovitis may be at risk of a destructive course irrespective of the JIA onset subtype.

Key words

Juvenile idiopathic arthritis, radiographic damage, radiographic progression, wrist.

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Introduction

In juvenile idiopathic arthritis (JIA), the wrist is the most commonly involved joint in the upper limbs (1) and, after the knee, the commonest joint in the body, being affected in roughly 60% of patients (2,3). Wrist involvement is detectable within one year of disease onset in the majority of cases (4). In our series of JIA patients, the frequency of wrist involvement in the first 2 years after disease presentation has been found to be 46% among those with extended oligoarthritis and 78% among those with rheumatoid factor (RF)-negative polyarthritis (unpublished observation). The wrist, together with the hip, is the most vulnerable site of radiographic changes in JIA(5, 6). Furthermore, wrist involvement has been associated with a more severe course of arthritis (7,8), a poorer functional outcome (6), or the lesser likelihood of a short-term therapeutic response (9).

With persistent disease activity, the wrist becomes affected bilaterally in most of the patients with polyarticular-onset JIA. At variance, in oligoarticular-onset disease, which is most commonly asymmetric, the wrist joint can be involved unilaterally (3). A high frequency of radiographic abnormalities in JIA patients with polyarthritis and bilateral wrist disease has been reported (10-12). It is unclear, however, whether patients with unilateral wrist involvement have a similar risk of joint damage.

In the present study, we describe the clinical and radiographic features of 6 JIA patients who developed unilateral destructive wrist synovitis.

Patients and methods

Patient selection

Beginning in December, 1986, all consecutive patients who fulfilled the revised International League of Associations for Rheumatology (ILAR) criteria for JIA (13), and who had wrist joint involvement underwent a bi-annual clinical assessment and a yearly bilateral wrist radiograph. No patient was excluded or declined to participate in the study protocol. For the purposes of this study, all wrist films were retrospectively reviewed to identify patients who developed unilateral erosive wrist synovitis, defined as is indicated below.

Clinical assessment

The general patient and disease characteristics included: sex, onset age, onset type, course type, disease duration, antinuclear antibodies (ANA), RF, iridocyclitis, second-line drug therapies, intraarticular corticosteroid injections in the affected wrist, dominant hand, joints involved other than wrist, and radiographic changes (joint space narrowing and/or erosions) in joints other than wrist.

The following assessments were made at baseline and every 6 months until the end of the study: physician's global assessment of overall disease activity measured on a 10-cm visual analogue scale (VAS) (0 = no activity; 10 = maximum activity); parent's global assessment of the child's overall well being on a 10-cm VAS (0 = very good; 10 = very poor); Childhood Health Assessment Questionnaire (CHAQ), Italian version (14) (0 = best; 3 = worst); number of swollen joints; number of joints with pain upon movement/tenderness; number of joints with limited range of motion (LROM); number of joints with active arthritis (defined as the number of joints with swelling or, if no swelling was present, with limitation of movement with either pain upon movement or tenderness); erythrocyte sedimentation rate (ESR) (Westergren method); and C-reactive protein (CRP) (nephelometry). The articular indices were assessed in a total of 67 joints (those that are included in the normal clinical evaluation), as previously reported (15).

In the first years of the study, functional ability was measured using either the Modified Lee Index (16) or the Juvenile Arthritis Functional Assessment Report (JAFAR) (17). In order to standardise scores from all functional ability tools, scores from the JAFAR and the Modified Lee Index were proportionally converted to the 0-3 scale of the CHAQ. Because we previously observed a very high correlation among the 3 instruments when administered to the same patient on the same day (15),

we felt justified in combining scores from the different instruments for purposes of analysis.

To quantify the impairment in wrist function at the last follow-up visit (that coincided with the last wrist radiograph), a LROM score was calculated for each wrist by grading the range of the 4 wrist movements (flexion, extension, ulnar deviation and radial deviation), as follows: 0 = full range; 1 = 1 – 25% limitation; 2 = 26–50% limitation; 3 = 51–75% limitation; 4 = 76–100% limitation, as previously reported (15). Furthermore, the CHAQ scores for the 4 areas that mostly involve wrist function (Dressing and Grooming, Eating, Hygiene, Grip) was calculated and was defined as wrist-CHAQ. As for the complete CHAQ, the scores for each of the 4 functional areas were averaged to calculate the wrist-CHAQ score, which could also range from 0 to 3 (0 = best; 3 = worst).

To be considered as ANA or RF positive, patients had to have at least 2 positive tests made at least 3 months apart. The ANA test was considered positive when the titre was ≥1:160 in indirect immunofluorescence on Hep-2 cells and the IgM RF test was considered positive when the titre was above 40 mg/dl on nephelometry.

Radiographic assessment

Standard radiographs of both wrists in posteroanterior view were made using a 3M XDA film and a 3M Trimax T16 cassette. The x-ray setting was 50 mA, 0.03 seconds, 43 to 47 kV. Radiographic damage was scored according to the Poznanski's method (18), as reported (11). Briefly. this method is based on the measurement of the radiometacarpal length (RM), which is the distance from the base of the third metacarpal bone to the midpoint of the distal growth plate of the radius, and of the maximal length of the second metacarpal bone (M2). The RM and M2 measurements were taken to the nearest 0.1 mm by using a precision gauge (Dial, Switzerland).

Because JIApatients are often small for their age and their bones are correspondingly small, age related standards are not reliable. In the Poznanski method, therefore, the carpal width (RM) is compared to an adjacent bone length (M2) rather than with age. Indeed, it is believed that the RM is more closely correlated to stature than to age, and stature correlates well with M2. This approach allows a measure of joint size that is relatively independent of the size of the child.

The measures obtained for RM and M2 were plotted against each other on the normative charts of Poznanski *et al.* (18). For each wrist, the number of standard deviations (SD) between the expected and the observed RM for the measured M2 was calculated according to the formulae reported by Poznanski *et al.* (18). The RM/M2 score, which represents the carpal length and will be referred to as the "Poznanski score", reflects the amount of radiographic damage in the wrist. The more negative the Poznanski score is, the more severe the radiographic damage. For this study, a Poznanski score below –2 units was defined as abnormal. In our hands, the inter and intra-reader agreement for Poznanski score measurement ranged from 0.97 to 0.99 (11).

Unilateral erosive synovitis was defined as a difference of at least –3 units in the Poznanski score between the affected wrist and the unaffected wrist, with the Poznanski score in the unaffected wrist being > – 2 units throughout the follow-up period.

The radiographic progression in the whole follow-up was then determined for each patient by calculating the change in the Poznanski score between the baseline and the final radiograph. Because the length of follow-up was variable among patients, the radiogra-

Table I. Clinical features of the study patients.

Patient No.	1	2	3	4	5	6
Sex	F	F	F	F	F	F
Onset age (years)	4.2	1	1.8	10.6	1.6	1.3
Disease duration[$]	11.6	4.2	6.8	3	16	2
Onset type	Polyarticular	Oligoarticular	Oligoarticular	Oligoarticular	Oligoarticular	Oligoarticular
Course type	Polyarticular	Polyarticular	Polyarticular	Polyarticular	Polyarticular	Polyarticular
Antinuclear antibodies	Pos	Pos	Pos	Neg	Pos	Pos
Rheumatoid factor	Neg	Neg	Neg	Pos	Neg	Neg
Iridocyclitis	Yes	Yes	Yes	No	No	No
Second-line drugs	MTX, SSZ, CyA, etanercept	MTX	MTX, SSZ, CyA, etanercept	MTX	MTX, SSZ, CyA	MTX
No. IAC wrist injections	2	-	3	1	1	-
Site of the affected wrist	Right	Right	Left	Right	Right	Left
Dominant hand	Right	Right	Right	Right	Right	Right
Joints involved other than wrist*	E*, H, Hi*, K, A, F	E, H, Hi*, K, A	CS, S, E, Hi, K, A, F	H*, K, A, F	H, K, T	H, K, A

[$] from the disease onset to the last observation; * joint with radiographic damage (i.e. with joint space narrowing and/or erosions); MTX: methotrexate; SSZ: sulfasalazine; CyA: cyclosporine A; IAC: intraarticular corticosteroid; S: shoulder, E: elbow, H: hand small joints; Hi: hip; K: knee; A: ankle; F foot small joints; CS: cervical spine; T: temporo-mandibular joint.

phic change between the baseline and the final radiographs was divided by the years of follow-up, thus obtaining the yearly radiographic progression. A positive value of radiographic progression indicates improvement, whereas a negative value reveals worsening.

Results

During the study period – from December 1986 to December 2002 – approximately 900 wrist radiographs were taken for 250 patients. This group accounts for 62.5% of a whole cohort of roughly 400 JIA patients. A review of the entire radiograph sample showed that 6 patients had developed unilateral erosive wrist disease by the above criteria. All these patients were females. The age at disease presentation ranged from 1 to 10.6 years and the disease duration from disease presentation to the last follow-up visit ranged from 2 to 16 years. The JIA onset subtype was oligoarticular in 5 patients and polyarticular in 1 patient. In all patients the arthritis followed a polyarticular course. Five patients had positive ANA and 1 had positive RF. During the disease course, all patients received one or more second-line drugs and all but 2 received 1 or more intraarticular injections in the affected wrist. The corticosteroid preparation used was triamcinolone hexacetonide in all patients; the dose ranged from 7.5 to 15 mg. In the 4 patients who received joint injections, the time interval between the disease presentation and the first injection ranged from 1.9 to 13 years and the time interval between joint injections from 15 to 20 months; the Poznanski score before the first injection ranged from –2.39 to –5,06 units. Three of the 6 patients had erosive disease in joints other than wrist. In all but 2 patients, the dominant hand was affected. The main clinical features of the study patients are presented in Table I.

Table II shows the clinical measures of disease activity and disability and the radiographic data at the last follow-up visit. At the final observation, all patients had continued disease activity, as shown by the physician's and parent's global assessments ≥ 0.5, the presence of ≥ 1 active joints, and the persistent elevation of ESR and/or CRP in 4 of the 6 cases. The clinical indicators of physical disability were also abnormal in all patients, with a CHAQ score ≥ 0.375 and ≥ 1 joints with LROM. All patients had some impairment in wrist function, as indicated by a wrist-CHAQ score ≥ 0.25 and a LROM score ≥ 1 in the affected wrist. Two patients had wrist subluxation.

There was a marked radiographic damage in all of the affected wrists; the Poz-

Table II. Measures of disease activity and disability and radiographic data at the last follow-up visit.

Patient no.		1	2	3	4	5	6
Physician's global assessment[#]		8	0.5	5.8	8.7	1.7	5.3
Parent's global assessment[#]		4.8	2.1	3	3.8	3.2	6.8
Parent's pain assessment[#]		5	0.9	1.9	4.4	1.2	8.5
No. active joints		5	1	7	11	3	6
Erythrocyte sedimentation rate (mm/h)		13	13	52	52	14	51
C-reactive protein (mg/dl)		< 0.3	< 0.3	2.4	1.3	1.6	2.3
CHAQ score[$]		0.625	0.375	1.6	0.875	1.5	1.25
Wrist-CHAQ[§$]		0.5	0.25	1.75	0.75	1.5	1.5
No joints with LROM		6	1	10	5	5	3
Wrist LROM score	Unaffected wrist	1	0	0	0	0	0
	Affected wrist	3	1	3	2	4	1
Poznanski score	Unaffected wrist	- 1.76	1.06	- 0.07	- 0.96	- 1. 49	- 0.84
	Affected wrist	- 8.35	- 2.39	- 5.55	- 8.50	- 8.02	- 3.12
Yearly radiographic progression	Unaffected wrist	- 0.12	- 0.09	- 0.10	0	0.02	-[£]
	Affected wrist	- 0.70	- 0.32	- 0.87	- 1.72	- 0.36	-[£]

[#]Score range: 0 = best to 10 = worst; CHAQ: Childhood Health Assessment Questionnaire; [§]Score of CHAQ areas involving wrist function; [$]Score range: 0 = best to 3 = worst; LROM: limited range of motion; [£] only 1 wrist radiograph was available.

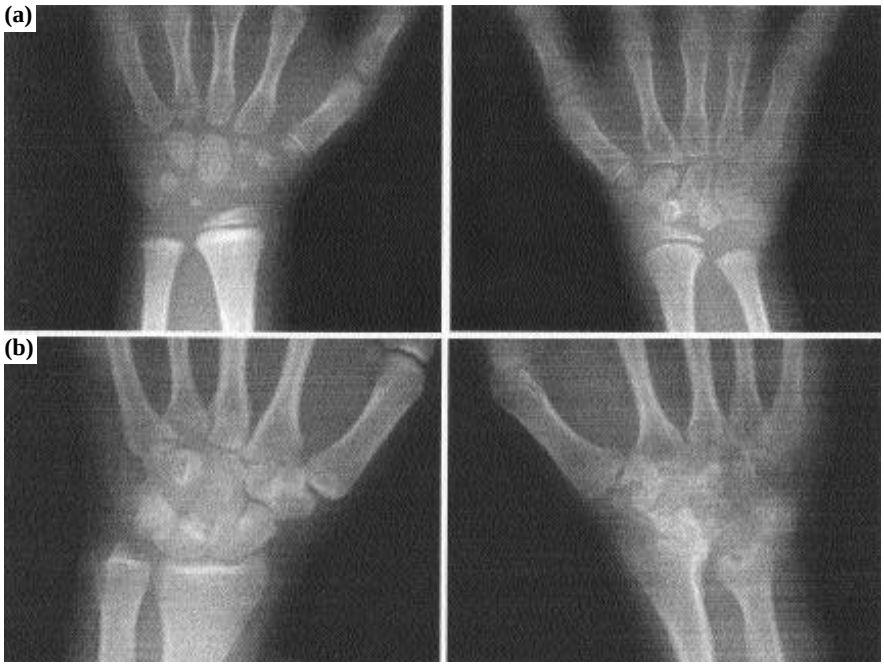

Fig. 1. Patient #5. (**a**) Wrist radiograph at 3 years after disease onset showing joint space narrowing in the right wrist (Poznanski score: –3.7 units). (**b**) Wrist radiograph at 16 years after disease onset showing advanced destructive changes in the right wrist (Poznanski score: –8.0 units). The yearly radiographic progression rate between the two radiographs is 0.02 in the left wrist and –0.36 in the right wrist.

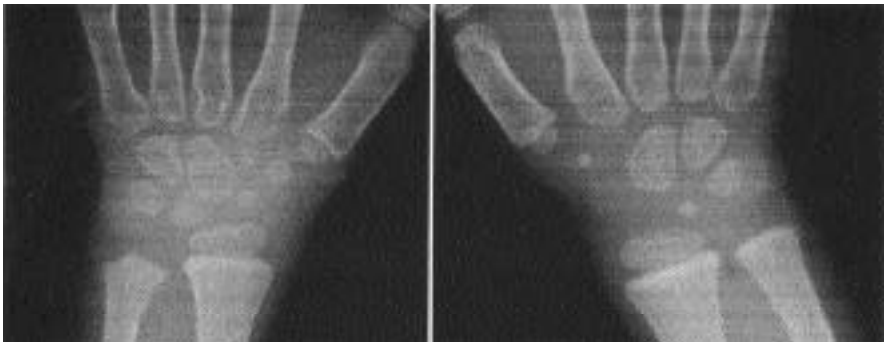

Fig. 2. Patient #6. Wrist radiograph at 2 years after disease onset showing acceleration of the bone age and erosions in the base of the third metacarpal bone on the left side and normal findings on the right side. The Poznanski score is –0.8 units in the right wrist and –3.1 units in the left wrist.

nanski score ranged from -8.0 to -8.50 units in 3 patients, and was -5.5, -3.1 and -2.4 units, respectively, in 3 patients. The lowest Poznanski scores corresponded to the presence of severe erosive changes in the carpal bones (Fig. 1). The severity of radiographic damage in the ANA-positive patients with longer disease duration (patients #1 and #5) was comparable to that observed in the RF-positive patient (patient #4). The destructive potential of wrist disease is exemplified in Figure 1, which shows the progression of radiographic damage over 13 years in patient #5. As shown in Figure 2, an early sign of unilateral erosive wrist arthritis in these patients can be the development of an apparent advanced bone age in the affected wrist.

Discussion

Although wrist involvement is common in JIA, unilateral erosive wrist disease seems to be rare, as it was found in only 6 of 250 patients who received approximately 900 wrist radiographs. We must acknowledge that this may not represent the true incidence of this feature because some patients who had wrist involvement on clinical grounds had a too short disease duration to allow detection of radiographic changes and in some other patients the progression of structural damage could have been slowed or halted by intraarticular corticosteroid and/or second-line therapies. We also recognize that the clinical meaning of our findings is limited by the small size of the patient sample.

Nevertheless, this patient group is worth describing because the erosive potential of synovitis in the affected wrist was comparable to that observed in our JIA patients with more severe bilateral wrist disease. Indeed, in these patients the Poznanski score in the affected wrist after a median of 5.5 years of disease duration (median –5.5 units; range –8.5 to –2.4 units) was in the low range of that recorded by us in 94 patients with bilateral wrist involvement after a median of 4.5 years of disease duration (median–1.6 units; range –9.7 to +2.2 units) (11). Notably, the severity of radiographic damage in the 2 ANA-positive patients with the longest disease duration was comparable to that detected in the patient who had positive RF, which is a predictor of poorer outcome in JIA (19). This latter patient appears to have an unusual form of oligoarticular onset JIA, which is characterized by the presence of RF, relatively late disease onset, and early erosive disease (20). The severity of arthritis in these patients is also demonstrated by the fact that all experienced a polyarticular course and had continued disease activity at the last follow-up visit. All patients were right-handed and in all but two patients the dominant side was affected. Although the relationship of hand use and joint destruction is not clearly defined (21,22), significantly greater joint destruction in the dominant hand has been reported in adult patients with rheumatoid arthritis (23). Notably, radiographic progression is one of the most important outcome measures in JIA and joint damage and disability may both increase with disease duration, although their link is uncertain (24, 25).

Because of its complicated structure, the wrist is prone to deformity, which can subsequently lead to disability of the hand. In our patients, joint damage was always accompanied by functional impairment and, in 2 cases, by wrist subluxation. This indicates that these patients deserve a careful radiographic follow-up and an early aggressive therapy aimed at suppressing joint inflammation in the wrist to prevent progression of radiographic damage and development impaired range of motion and joint deformity. Evans *et al*. (3) reported encouraging results of intraarticular corticosteroid injection therapy in the prevention of wrist deformity. Another suggested approach to preserve wrist function is splinting in the affected joint (2, 3). Unilateral erosive wrist disease may represent an indication for early introduction of second-line treatment.

As observed in our patients, the detection of an apparent advanced bone age in the affected wrist may represent an early sign of unilateral erosive wrist arthritis. This phenomenon is due accelerated maturation of bones resulting from inflammatory hyperemia (26). It has been reported that the first bony change on wrist X-ray in JIApatients is premature appearance of carpal bones, which can be accompanied by narrowing of the intercarpal joint spaces (3). Early diagnosis of erosive disease can also be facilitated by serial measurements of the Poznanski score, which is a measure of cartilage loss. We have recently shown that the early Poznanski score change predicts subsequent radiographic progression and long-term joint damage and disability (11).

In summary, we have described a distinct subgroup of JIA patients characterized by the development of unilateral destructive wrist synovitis. In these patients, who are most frequently ANA-positive, the occurrence of an asymmetrical accelerated bone age in the affected wrist may represent an early sign of erosive disease.

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