Palindromic Rheumatism Is a Common Disease: Comparison of New-Onset Palindromic Rheumatism Compared to New-Onset Rheumatoid Arthritis in a 2-Year Cohort of Patients

ANNE POWELL, PAUL DAVIS, NIALL JONES, and ANTHONY S. RUSSELL

ABSTRACT. ***Objective.*** To determine the prevalence of palindromic rheumatism (PR) compared to new-onset rheumatoid arthritis (RA).

Methods. We reviewed 145 patients that had been newly diagnosed by a rheumatologist with either RA or PR between May 2004 and May 2006.

Results. Of these 145 patients, 51 were diagnosed with PR and 94 with RA. There was a similar female predominance with both conditions. The average age at diagnosis of PR was 49 years as compared to 56 years for RA.

Conclusion. Palindromic rheumatism occurs more frequently than previously recognized. (First Release April 15 2008; J Rheumatol 2008;35:992–4)

Key Indexing Terms:
PALINDROMIC ARTHRITIS RHEUMATOID ARTHRITIS PREVALENCE

Palindromic rheumatism (PR) was originally described in 1944 by Hench and Rosenberg, who reported 34 patients with the condition. It was described as a condition of multiple afebrile attacks of acute arthritis and periarthritis, and sometimes also of para-arthritis, with pain, swelling, redness, and disability generally of only 1, but sometimes of more than 1, small or large joint in an adult of either sex[1]. The condition had little or no constitutional reaction or abnormality by laboratory tests and no significant functional, pathologic, or radiological changes even after years of disease. In a Finnish survey of 60 patients with PR, it was felt that the syndrome was often ignored or misdiagnosed by the physician. They suggested diagnostic criteria to be recurrent attacks of sudden onset mono- or polyarthritis or periarticular tissue inflammation lasting from a few hours to 1 week; verification of at least 1 attack by a physician; subsequent attacks in at least 3 different joints; and finally, exclusion of other forms of arthritides[2].

The exact prevalence of PR is difficult to determine, but in a retrospective cohort of 4900 patients with musculoskeletal (MSK) disorders seen by 3 rheumatologists at our center over a 10-year period, 127 were found to have PR at the time of review[3]. In another study, the frequency was estimated to be only one-twentieth that of RA[4]. The age of onset has been described as 40 ± 12 years in one cohort and 36 years in another[3,5]. In the original description, there was no clear female predominance as seen in RA[1]. However, in a later cohort with PR, 65% were female, which is more in keeping with the sex distribution of RA[3]. In the original cohort, upper limbs were affected more commonly than the lower limbs[1]. In a study of patients with PR, 28/32 (88%) had hand involvement[6]. Joints frequently affected in another cohort were wrist, knee, and metacarpophalangeal (MCP) joints[3].

In the original description by Hench and Rosenberg, the erythrocyte sedimentation rate (ESR) was normal in 40%, slightly increased in 48%, and moderately increased in 12%[1]. In another cohort of patients with PR, 18/32 (56%) were positive for cyclic citrullinated peptide (CCP)[6].

The primary objective of our study was to compare the incidence of PR, diagnosed by a rheumatologist, with that of RA. Secondary objectives were to reassess the observations by Hench and Rosenberg, and to observe differences in time to diagnosis, age, sex, joints affected, results of investigations done, and treatment started.

MATERIALS AND METHODS

We conducted a cross-sectional study based on a review of medical records in patients referred to 3 rheumatologists, 2 in an academic center and 1 in the community in Edmonton, Canada. By using their databases, we identified patients with a diagnosis of either RA or PR who were seen the first time during a 2-year period from May 2004 to May 2006. These charts were then reviewed and excluded if the diagnosis had been made by a rheumatologist prior to May 2004, or was subsequently shown to be incorrect. Any patients who progressed from PR to RA during the study would

From the University of Alberta, Edmonton, Alberta, Canada.

A. Powell, MD; P. Davis, FRCP, Professor of Rheumatology; N. Jones, FRCP, Clinical Associate Professor of Rheumatology; A.S. Russell, FRCP, Professor of Rheumatology, University of Alberta.

Address reprint requests to Prof. A.S. Russell, University of Alberta, 562 Heritage Medical Research Center, Edmonton, AB T6G 2S2.

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have retained their original diagnostic category. Similarly, those who presented with RA, but had previously, by history, had PR, were categorized as new RA for the purposes of our study. The diagnosis of PR was based on acute pain and swelling in at least 1 joint for a period up to a maximum of 7 days[7]. All patients had had at least 3 episodes. The diagnosis of RA was accepted if made by a physician as definite RA and treated accordingly.

Antinuclear antibody (ANA) testing was by indirect immunofluorescence, and the cutoff titer for a positive result has been held over the years at 1/40, but in this laboratory the sensitivity has been decreased deliberately so that only 7% of the normal population is positive at this titer[8]. CCP antibodies are assessed with an anti-CCP2 technique[7]. Rheumatoid factor (RF) testing was carried out in the hospital laboratory by a commercial latex agglutination test, a positive titer being over 1/20.

RESULTS

The numbers of patients in each group are described in Table 1. There is some variation between the rheumatologists; however, this does not appear to be attributable to an academic versus a community setting. Table 2 shows that the distribution in regard to sex is similar between PR and RA, with 64% of those with PR being women compared with 69% with RA. The age at diagnosis ranged from 29 to 85 years, with an mean age of 49 years for PR and 56 years for RA. Disease modifying antirheumatic drug (DMARD) treatment was initiated at first consultation in 44/51 (86%) PR and 92/94 (98%) RA patients. The most common treatment used for PR was an antimalarial. Common initial treatments for RA were antimalarials and/or methotrexate (MTX). Biologics were not initiated for either PR or RA at first diagnosis. Table 3 shows the joints that have been affected in these patients. It shows a high percentage of hand involvement in PR, at 81%, but also shows significant lower-limb distribution as well. While all patients had had at least 3 attacks, many had many more than this so that it was often impossible to reliably estimate their number or frequency and these data are not included.

Table 1. Number of cases reviewed, by setting.

	Academic 1	Academic 2	Community	Total
PR, n (%)	32 (44)	4 (26)	15 (27)	51 (35)
RA, n (%)	41 (56)	11 (74)	42 (73)	94 (64)

PR: palindromic rheumatism; RA: rheumatoid arthritis.

Table 2. Distribution of palindromic rheumatism (PR) and rheumatoid arthritis (RA).

	PR	RA
Male, n (%)	17 (34)	29 (31)
Female, n (%)	33 (64)	65 (69)
Average age at diagnosis, yrs	49 (22–85)	56 (22–87)
Mean duration of symptoms, mo	42 (1–492)	15 (1–264)
ESR, mm/h	22	32
CRP, mg/l	9.3	24.3
ANA positivity, n (%)	18 of 35 tested (51)	29 of 64 tested (45)
RF positivity, n (%)	21 of 40 tested (53)	54 of 88 tested (61)
CCP positivity, n (%)	18 of 37 tested (49)	28 of 47 tested (60)
Treatment initiated, n (%)	47 of 51 (92)	92 of 94 (98)
NSAID, n (%)	4 of 51 (8)	4 of 94 (4)
Antimalarial, n (%)	42 of 51 (82)	62 of 94 (67)
MTX, n (%)	0 of 51	41 of 94 (44)
Other DMARD, n (%)	2 of 51 (4)	9 of 94 (10)
Prednisone, n (%)	0 of 51	8 of 94 (9)

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ANA: antinuclear antibodies; RF: rheumatoid factor; CCP: cyclic citrullinated peptide; NSAID: nonsteroidal antiinflammatory drugs; MTX: methotrexate; DMARD: disease modifying antirheumatic drugs.

DISCUSSION

A previous study, while emphasizing the importance of PR, suggested a frequency of 5% of that of RA[4]. However, in our 2-year cohort, it was 10 times more frequent than this. Certainly, there was a variation between physicians, but all 3 physicians had much higher rates than previously reported. Many textbooks have surprisingly little information regarding the diagnosis or nature of PR. The *Oxford Textbook* does not even have it indexed[9]. The textbook *Rheumatology* has 2 equivalent paragraphs in different sections of about 12 lines[10]. The *Primer on the Rheumatic Diseases* and the older textbook, *Clinical Rheumatology*, do best with almost half a page[11,12].

Few of our patients received nonsteroidal antiinflammatory drug (NSAID) therapy, largely because it often has been tried unsuccessfully, but also it is our belief that NSAID use is only minimally helpful in reducing the pain and inflammation of an acute attack. Antimalarial use was frequent, to reduce the frequency of episodes as well as in the hope of preventing progression[5]. Corticosteroid injections were very rarely used, again, because of the self-limited nature of each attack. None of the patients in our study were noted to have progressed from PR to RA, but this is probably a reflection of relatively short followup duration. We were not able to determine accurately how many of the patients presenting as RA had previously had palindromic episodes.

The literature gave mixed information as to whether there was a sex difference, and our study confirms a female predominance similar to that of RA. The mean duration of symptoms is substantially longer in the palindromic group, which is probably explained by its intermittent and nondestructive presentation. As one might anticipate, given the high rates of progression to RA[7], the age of onset appears to be slightly lower than that of RA.

In terms of joints affected, the knee, wrists, and hands have been reported in the literature as the most commonly affected in PR. Our study supports that the hands are most commonly affected, and then the knee. The wrist was similar in frequency to shoulders and ankles; MCP and proximal interphalangeal joint involvements were seen by themselves but often in association with wrist involvement, and this was

Table 3. Affected joints in patients with palindromic rheumatism (PR) and rheumatoid arthritis (RA).

	Hands	Wrists	Elbow	Shoulder	Neck and Back	Hips	Knees	Ankles	Feet
PR: n = 48	39 (81)	14 (29)	8 (17)	13 (27)	0 (0)	7 (15)	24 (50)	14 (29)	18 (38)
RA: n = 92	80 (87)	42 (46)	18 (20)	31 (34)	3 (3)	5 (5)	47 (51)	23 (25)	57 (62)

All values are n (%).

not always distinguished in the charts. The feet, which have not been previously reported as a common area being affected in PR, were the third most common area affected.

In terms of investigations, the inflammatory markers were generally higher in new-onset RA, but were often elevated in PR also. The rates of RF and CCP positivity were slightly higher in RA, but there were still substantial numbers in the palindromic group, as described[6,7].

Most patients in both groups began receiving therapy. Many patients in the RA group were given combination therapy. The most common therapy for PR appears to be antimalarials, and for RA it included MTX.

Our study can give no true incidence or frequency rates, but the comparison with incident RA allows at least a relative estimate. Previous studies from our unit suggest approximately 50% of these patients with PR may progress to overt RA. We have not addressed this issue again here.

The cause of PR remains unclear and whether our findings can be extrapolated to other ethnic groups or other environments is uncertain. The short waiting lists in Edmonton for inflammatory arthritis may partially explain our higher rates of PR; i.e., we see these patients before progression to RA. Rheumatology textbooks appear to project a distorted view of the frequency of PR. Given the current emphasis on recognizing and treating RA early, the recognition of PR as well as undifferentiated arthritis as a form of "pre-rheumatoid arthritis" may be important in providing such a window of opportunity.

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