

## Examination of IgM Rheumatoid Factor (IgM-RF) and Anti-cyclic Citrullinated Peptide Antibody (Anti-CCP Ab) in Japanese Patients with Palindromic Rheumatism

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### Abstract

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We have studied the serology of 6 patients with palindromic rheumatism. None of the patients fulfilled the classification criteria for rheumatoid arthritis at the entry; however, 4 out of the 6 patients were seropositive for IgM rheumatoid factor (IgM-RF) at entry. Sequential serological study was performed in 4 patients; IgM-RF changed from seronegative to seropositive in one patient, and the titer increased in another patient. Anti-cyclic citrullinated peptide antibody (anti-CCP Ab) at the entry was detected in only one of the 6 patients; that patient later developed RA. Although follow-up is necessary, the present study may suggest the importance of serological examination, especially anti-CCP Ab, in patients with palindromic rheumatism.

**Key words:** palindromic rheumatism, IgM-RF, anti-CCP Ab

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### Introduction

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Palindromic rheumatism is characterized by recurrent attacks of acute arthritis of short duration. In the long term, some of these patients develop a connective tissue disease, usually rheumatoid arthritis (RA) (1, 2). Previous studies in Europe and North America showed that the presence of IgM rheumatoid factor (IgM-RF) in palindromic rheumatism patients indicates a future risk for RA (1-4), and anti-cyclic citrullinated peptide antibody (anti-CCP Ab) was recently reported in palindromic rheumatism patients (5). Thus, we measured IgM-RF and anti-CCP Ab in the sera of Japanese palindromic rheumatism patients.

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### Case Presentation

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We encountered 6 patients with palindromic rheumatism,

as diagnosed by the criteria described by Gonzalez-Lopez et al (1). Informed consent was obtained from all of the patients.

Table 1 summarizes the profiles of the 6 palindromic rheumatism patients. All patients were prospectively followed-up, and the disease duration was estimated from the time of first attack until the last consultation. Seropositivities of IgM-RF and anti-CCP Ab shown in Table 1, were obtained from the data of the latest serological examinations. Joint involvement in Table 1 shows the total joints affected during the follow-up period. Serology was serially examined in 4 patients; IgM-RF turned to be positive in one patient and its titer increased in one case (Fig. 1). Among the 6 patients, one patient developed RA later. IgM-RF was seropositive in 4 out of 6 patients; however, only the one patient who developed RA was positive for anti-CCP Ab. Anti-CCP Ab in this case was consistently positive; however, IgM-RF was negative during the follow-up period

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**Table 1.** Clinical Findings and Serological Data from 5 Patients with Palindromic Rheumatism

	Age (yr)	Sex (M/F)	Affected joints	Disease Duration (M)	IgM-RF (IU/ml)	Anti-CCP Ab (U/ml)
Case 1	58	M	ankle, MTP	19	98.6	0.6
Case 2	51	F	wrist, shoulder, ankle, knee	64	<9.8	<0.6
Case 3	40	F	wrist, MCP, PIP	24	90.0	0.6
Case 4	68	M	wrist, elbow, ankle, knee	88	37.0	3.0
Case 5	63	M	wrist, elbow, ankle	22	28.0	<0.6
Case 6	52	M	shoulder, ankle, wrist	7	<9.8	72.0

IgM-RF was measured by latex-enhanced immunoelectrometric assay (Dade Behring, Marburg, Germany, cut-off value=14 IU/ml). Anti-CCP Ab was measured by enzyme-linked immunosorbent assay (DIASTAT Anti-CCP, Axis-Shield, Dundee, UK, cut-off value=4.5 U/ml). IgM-RF was positive in cases 1, 3, 4 and 5, whereas anti-CCP Ab was positive in case 6.

(Fig. 1 and Table 1). Plain radiographs of the affected joints were examined serially (case 1 to case 6), but no erosive bone changes were not found in any of the patients (data not shown).

## Discussion

Gonzalez-Lopez et al have reported that 28% of patients with palindromic rheumatism developed RA after a mean follow-up of 6 years (1). Previous investigations including that of Gonzalez-Lopez et al showed that seropositivity for IgM-RF could be one of the risk factors for subsequent development of RA (1-4). The present study includes 6 cases with a mean follow-up of 3.1 years. Among them, the one patient who developed RA later was seropositive for anti-CCP Ab and seronegative for IgM-RF. Thus, the presence of anti-CCP Ab might be a prognostic factor for future onset of RA. The involvement of proximal interphalangeal (PIP) joints, wrist joints and metacarpophalangeal (MCP) joints has been suggested to indicate future risk for RA in patients with palindromic rheumatism (1), and such involvement was observed in 5 out of 6 patients. Thus, further follow-up will be necessary to detect the onset of RA of our cases.

Van Gaalen et al recently revealed that the presence of anti-CCP Ab is the best predictor for the progression to RA in patients with undifferentiated arthritis (6). Anti-CCP Ab is reported to be found in 56.3% of patients with palindromic rheumatism in Spain (18 out of 32 patients); however, prediction of the future development of palindromic rheumatism to RA by anti-CCP Ab remains to be determined (5). Our prospective study of early-stage RA indicates that about 70% of the patients at baseline already show the seropositiv-

Case 2	2000 February	2003 March	2003 July	2004 April	2005 March
	onset ↓	↓	↓	↓	↓
IgM-RF (IU/ml)	<9.8	<9.8	<9.8	<9.8	<9.8
Anti-CCP Antibody (U/ml)	N.T.	1.4	N.T.	1.2	<0.6
Case 3	2003 August	2004 April	2005 April		
	onset ↓	↓	↓		
IgM-RF (IU/ml)	38	70	90		
Anti-CCP Antibody (U/ml)	1.2	1.2	0.6		
Case 4	1998 February	2001 February	2002 September	2005 February	
	onset ↓	↓	↓	↓	
IgM-RF (IU/ml)	<9.8	<9.8	23	35	
Anti-CCP Antibody (U/ml)	N.T.	N.T.	N.T.	3.0	
Case 6	2005 March	April	August	October	
	onset ↓	↓	↓ RA	↓	
IgM-RF (IU/ml)		<9.8		<9.8	
Anti-CCP Antibody (U/ml)		135		72.0	

**Figure 1.** Serial serological examinations of 4 patients with palindromic rheumatism. IgM-RF: IgM rheumatoid factor. Anti-CCP Ab: anti-cyclic citrullinated peptide antibody. N.T.: not tested. In case 2, the patient's condition developed into persistent arthritis in July 2003, whereas she did not fulfill the 1987 ACR classification criteria for RA. In addition, plain radiographs of the affected joints did not show any erosive change until now. In case 6, the patient was diagnosed as RA in August 2005; however, plain radiographs of the affected joints in October 2005 did not show any erosive change.

ity with anti-CCP Ab (7, 8); the difference in anti-CCP Ab seropositivity from that found by Salvador et al (5) in Spain may be due to arise from racial difference. Further study may answer question.

The present data are preliminary and limited; however, to our knowledge, this is the first prospective observation of Japanese patients with palindromic rheumatism regarding IgM-RF and anti-CCP Ab. Further clinical investigation, including a large number of patients will be necessary to clarify the significance of IgM-RF and anti-CCP Ab in the prediction of further onset of RA in Japanese palindromic rheumatism patients.

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**Abbreviations:** ACR: American College of Rheumatology, anti-CCP Ab: anti-citrullinated peptide antibody, IgM-RF: IgM rheumatoid factor, MCP joint: metacarpophalangeal joint, MTP joint: metatarsophalangeal joint, PIP joint: proximal interphalangeal joint, RA: rheumatoid arthritis

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