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ORIGINAL ARTICLE

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Clinical and immunological features of systemic lupus erythematosus complicated by Jaccoud's arthropathy

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Abstract This work was undertaken to evaluate clinical and immunological features in patients with systemic lupus erythematosus (SLE) complicated by Jaccoud's arthropathy. Patients diagnosed with SLE between 1985 and 1999, and who met the criteria of Villiaumey et al., were checked for Jaccoud's arthropathy. Clinical features were retrospectively analysed for patients with both diseases. Sjögren's syndrome and human leukocyte antigens (HLA) in these patients were evaluated. Jaccoud's arthropathy was found in 15 (4.4%) of 340 patients with SLE. The mean age at the time of SLE diagnosis was significantly higher in these patients than in our control SLE patients, which was 51.2 ± 13.0 years ($n = 15$) and 29.6 ± 13.0 years ($n = 222$) ($p = 2.1 \times 10^{-8}$). Sjögren's syndrome was diagnosed according to the European Community Study Group's criteria in 10 (91%) of 11 patients examined. The incidence of HLA-A11 (5/9, 55%) and -B61(40) (5/9, 55%) in patients with Jaccoud's arthropathy was higher in the Japanese population (A11, 17.4%, $p < 0.05$; B61, 17.5%, $p < 0.057$. Jaccoud's arthropathy in patients with SLE is associated with Sjögren's syndrome, elderly SLE, HLA-A11, and HLA-B61. These clinical features might be characteristic of patients with Jaccoud's arthropathy and SLE.

Key words HLA · Jaccoud's arthropathy · Sjögren's syndrome · Systemic lupus erythematosus (SLE)

Introduction

Nonerosive arthropathy with marked articular dislocation or subluxation was first described by Jaccoud[1] in patients with rheumatic fever. Later investigators have reported complications of Jaccoud's arthropathy (JA) in other rheumatic diseases, including scleroderma, mixed connective tissue disease, and especially systemic lupus erythematosus (SLE). Several studies have suggested an association of sicca syndrome with SLE complicated by this specific arthropathy, although the diagnosis of Sjögren's syndrome (SS) in these patients is unclear in the literature.[2,3]

Jaccoud's arthropathy frequently affects the hands and feet, but rarely the ankles, elbows, shoulders,[4] or knees.[5,6] Pathological studies have revealed mild synovitis and inflammatory capsular fibrosis, which might be responsible for the characteristic deformities.[3,4,7–9] Since the diagnostic criteria of Jaccoud's arthropathy were proposed, this articular condition has been estimated to manifest in 4%–8% of patients with SLE,[10,11] although little is known about whether or not a difference in clinical features exists between SLE patients with and without arthropathy.

We describe the clinical and immunological aspects of patients in our institute with SLE and Jaccoud's arthropathy over a 15-year period, with special reference to the evaluation of SS and human histocompatibility antigen (HLA) typing.

Patients and methods

Diagnosis of SLE and Jaccoud's arthropathy

Among the 340 patients registered at our institute between 1985 and 1999, and who were diagnosed as having SLE according to the 1982 American Rheumatism Association (ARA) criteria,[12] 15 had marked deforming arthropathy on the hands and feet but did not meet the 1987 ARA classification criteria for rheumatoid arthritis (RA).[13] However, these 15 patients fulfilled the criteria for Jaccoud's arthropathy proposed by Villiaumey et al.[3]

Diagnosis of Sjögren's syndrome

Eleven of 15 patients with SLE and Jaccoud's arthropathy completed a questionnaire to evaluate symptoms of

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xerophthalmia and xerostoma according to the European Community Study Group's diagnostic criteria.[14] These 11 patients were examined by Schirmer's test, the Saxon test, sialography, and lip salivary gland biopsy. Sialography was assessed according to the Rubin–Holt classification.[15] The focus score was evaluated in each tissue section. The focus was defined as an agglomeration of at least 50 mononuclear cells, and the focus score was defined as the number of foci in 4 mm^2 of glandular tissue according to previous descriptions.[14,16]

HLA typing

HLA were determined in 9 of 15 patients with SLE and Jaccoud's arthropathy by a lymphocyte cytotoxicity test (Terasaki–NIH–Standard method). The incidence of HLA antigens in these nine patients was compared with data obtained from the Japanese population[17], and from Japanese patients with SLE.[18,19] Statistical analysis was performed by χ^2 test with Yate's correction.

Results

Patient demography and profile of Jaccoud's arthropathy

The incidence of Jaccoud's arthropathy was estimated at 4.4% (15/340) in our patients with SLE. All of the 15 patients were female. The mean age at the time of diagnosis of SLE was 51.2 ± 13.0 years (n = 15) in Jaccoud's arthropathy patients, which was significantly higher than that in our control SLE patients: 29.6 ± 13.0 years ($n = 222$) ($p = 2.1 \times 10^{-8}$, Student's t-test) (Table 1).

Ulnar deviation and swan neck or button hole deformities on the hands had manifested in all 15 patients. A hallux valgus was observed in 12, and a Z finger deformity was noted in 6 of the 15 patients. These deformities were restored even after marked subluxation occurred. X-rays of the affected hands and feet showed that no patient had bone erosion. Neither destructive and deforming changes nor loss of range of motion were observed in larger joints.

Early symptoms of Jaccoud's arthropathy consisted of morning stiffness and/or minimal to mild arthralgias. The mean ± SD duration from the initial joint symptoms to the typical deformity was 10.2 ± 3.3 years in the 15 patients. Established Jaccoud's deformities preceded the diagnoses of SLE by 4–10 years in six patients, or manifested 3–14 years after the diagnosis of SLE in nine patients. All six patients whose joints deformed prior to the diagnosis of SLE were misdiagnosed as having RA before being referred to us, despite lacking the classification criteria of RA.

Clinical aspects of SLE complicated by Jaccoud's arthropathy (Table 2)

Lupus nephritis was diagnosed histologically in 5 of 15 patients with Jaccoud's arthropathy, and no patients suffered from renal dysfunction. None of the 15 patients had a central nervous system (CNS) complication. Of our 222 control SLE subjects whose comprehensive hospital records were available, 21 had CNS lupus which required steroid therapy after excluding lupus headaches. The difference between incidences (0/15 and 21/222) was not significant. The rheumatoid factor was positive by latex agglutination in 60% (9/15) of the patients, although we did not have comparable data in our control SLE patients. Several investigators[3,8] have reported patients with Jaccoud's arthropathy who had a positive serum rheumatoid factor. However, Bywaters[4] proposed a seronegative as a criterion of Jaccoud's arthropathy. Hypergammaglobulinemia was common in all the 15 patients, with a mean of 2134 ± 711 mg/dl ± SD of the serum IgG level. Anti-Sm antibodies and anti-RNP antibodies were negative in all of the 15 patients.

Table 1. Demography of patients with Jaccoud's arthropathy and SLE

Patient, sex	Age when diagnosed with SLE (years)	Duration (years) from initial articular symptoms to:		Time from SLE to Jaccoud's deformity (years)
		Diagnosis of SLE	Jaccoud's deformity	
1 f	49	4	10	6
2 f	46	10	16	6
3 f	48	1	15	14
4 f	33	0	8	8
5 f	62	6	9	3
6 f	57	−6	3	9
7 f	52	20	10	−10
8 f	50	12	8	−4
9 f	75	14	10	−4
10 f	58	3	9	6
11 f	36	4	8	4
12 f	53	25	11	−14
13 f	74	24	15	−9
14 f	30	4	10	6
15 f	45	16	12	−4

Table 2. Clinical features of SLE in patients with Jaccoud's arthropathy

Patient	Malar rash	Discoid lupus	Photosensitivity	Oral ulcers	Arthritis	Serositis	Urine protein (WHO)	Lymphocytopenia	Anti-ds DNA (IU/ml)	ANA dilution (<10) ×
1	+	−	+	+	+	−	(−) class II	+	21	160 sp
2	−	+	−	−	+	−	(−)	+	24	640 h
3	+	−	−	−	+	−	(2+)	+	84	160 sp
4	−	−	−	−	+	−	(2+) class II	+	150	640 sp
5	−	+	−	−	+	−	(−)	+	37	160 sp
6	−	−	−	+	+	−	(−)	+	42	2560 sp
7	+	+	+	−	+	−	(3+) class V	+	13	640 sp
8	−	−	−	−	+	−	(1+) class II	+	11	2560 sp
9	−	−	−	−	+	+	(1+)	+	–	160 h
10	−	−	−	−	+	−	(1+)	+	14	2560 sp
11	−	−	−	−	+	−	(−)	+	100	2560 h
12	−	−	−	−	+	−	(−) class III	+	–	640 sp
13	−	−	−	−	+	−	(−)	+	15	40 sp
14	−	+	−	+	+	−	(−)	−	–	160 sp
15	−	−	−	−	+	−	(−)	+	18	160 sp

ANA, antinuclear antibodies; WHO, World Health Organization classification of renal histology
None of the patients had serum anti-Sm antibodies, biological false-positives, neuropsychiatric symptoms, thrombocytopenia, or autoimmune hemolytic anemia

Table 3. Complications of Sjögren syndrome

Patient	Ocular symptoms	Oral symptoms	Schirmer test	Lip biopsy	Saxon test	Sialography R–H stage	SSA (IU/mlI)	SSB (IU/mlI)
2	+	+	+	NT	+	II	NT	NT
3	+	+	+	+	+	III	15.3	−
4	+	+	+	+	+	IV	+[a]	NT
5	+	+	+	+	+	II	−	−
7	+	+	+	+	+	II	84	−
8	+	+	+	+	+	III	500	−
11	−	−	−	−	−	−	−	−
12	+	+	+	+	+	II	500	−
13	+	+	+	NT	+	NT	8	17.2
14	+	+	+	+	+	II	52	−
15	−	+	−	+	+	II	−	−

NT, not tested
[a] Ouchterlony (+)

Complication of Sjögren's syndrome

Four of the 15 patients were not followed-up at our hospital, but the other 11 were examined for Sjögren's syndrome. Xerophthalmia (82%, 9/11), xerostoma (91%, 10/11), a positive Schirmer's test (81%, 9/11), focus score ⩾1 on the salivary glands (88%, 8/9), and an abnormal sialogram (90%, 9/10) were common in these patients. Anti-SSA antibodies and anti-SSB antibodies were positive in 7 (70%) and 1 (11%) of the 11 patients, respectively (Table 3).

Sjögren's syndrome secondary to SLE was diagnosed in 10 (91%) of the 11 patients who had Jaccoud's arthropathy according to the European Community Study Group's criteria.

Among 115 SLE patients without Jaccoud's arthropathy in our institute between 1998 and 1999, Sjögren's syndrome was diagnosed in 18 (15.6%) according to the same criteria. Although the frequency of 91% (10/11) appears to be higher than 15.6% (18/115), we have not checked the frequency of Sjögren's syndrome in all of our patients with SLE.

Table 4. HLA typing in patients

Patient	HLA-A		HLA-B		HLA-C	HLA-DR	
3	11	24 (9)	51 (5)	61 (40)	3	ND	
5	11	31 (19)	51 (5)	60 (40)	7	4	10
7	2	31 (19)	54 (22)	61 (40)	1	ND	
8	26 (10)	24 (9)	52 (5)	61 (40)	3	2	9
11	11	24 (9)	39 (16)	52 (5)	7	2	9
12	11	24 (9)	54 (22)	61 (40)	1	4	
13	26 (10)	24 (9)		61 (40)	3	4	9
14	26 (10)	24 (9)	7		7	1	
15	11	2	51 (5)	54 (22)	1	2	4

ND, not detected

HLA typing (Tables 4 and 5)

The 55.5% frequency of HLA-A11 or -B61 in our nine patients with SLE and Jaccoud's arthropathy was significantly higher than that in the total Japanese population (relative risk = 5.9 and 5.9). The frequency of HLA-A11 or -B61 in our Jaccoud's arthropathy patients was

Table 5. Phenotype frequency (%) of HLA-A and HLA-B in patients and controls

HLA	Patients with JA and SLE ($n = 9$)	Japanese patients with SLE		Japanese population[17] ($n = 650$)
		Obana et al.[18] ($n = 34$)	Kameda et al.[19] ($n = 56$)	
A2	22.2	50.0	44.6	41.7
A11	55.5[a,b]	8.8[b]	32.1	17.4[a]
A24	66.6	61.8	37.5	63.0
A26	33.3	38.2	25.0	20.8
A31	22.2	14.7	17.8	16.6
B51	33.3	26.5	–	16.8
B52	22.2	11.8	16.0	22.9
B61	55.5[c,d]	38.2	23.2[d]	17.5[c]

[a] $P = 0.011$; [b] $P = 0.001$; [c] $P = 0.012$; [d] $P = 0.044$

higher than that in Japanese SLE patients, although these data[18,19] were based on small-scale studies.

Discussion

A 4.4% prevalence (15/340) of Jaccoud's arthropathy (JA) in our SLE patients was similar to those previously reported.[4,10,11]

We found a higher mean age at the time of SLE diagnosis in JA patients compared with our control SLE patients. The rarity of central nervous system involvement, renal dysfunction, and nephrotic syndrome in our JA patients might be compatible with that of elderly SLE patients who usually have a benign clinical course.[20,21] The high prevalence of Sjögren's syndrome (SS) in our patirets with JA and SLE was consistent with previous observations in which sicca syndrome was common. Furthermore, HLA-A11 and HLA-B61 precipitated in our patients with JA and SLE. These clinical features might be characteristic of patients with JA and SLE. Among previous reports on Japanese SLE and HLA,[18,19,22] an association between SLE and HLA-B39, DRB1*1501, DRB5*0101, and DQB1*0602 has been found.[22] Because only one out of nine patients with JA and SLE in the present study had HLA-B39, and we did not examined DNA typing of HLA in our patients, we could not compare the previous data[22] with ours.

To the best of our knowledge, the following studies have suggested an association between JA and secondary SS. Kramer et al.[2] reported that 12 of 14 patients with JA and SLE had a positive Schirmer's test and/or keratoconjunctivitis. Russell et al.[8] described five of seven patients with nonerosive deforming arthropathy and SLE who had keratoconjunctivitis sicca. Villiaumey et al.[3] reported six patients with sicca syndrome out of ten patients with JA and collagen diseases. Alarcon-Segovia et al.[23] described an association between deforming arthropathy and SLE complicated by SS, although they used deforming arthropathy in a broad sense, although JA was found in only 5 of the 41 patients. A patient with SS[24] or probable SS[25] has been described in a case report of SLE complicated by JA. In a case report by Chevalier et al.,[26] it was unclear whether JA was related to primary SS or secondary SS: a 41-year-old woman developed benign intracranial hypertension, which was attributed to SLE 7 years after the diagnosis of primary SS. Jaccoud's deformity preceded her CNS lupus by 4 years.

Villiaumey et al.[3] discussed the possibility that lacrimal and salivary gland involvement in SS could reflect a systemic disorder, including synovial inflammation, which might lead to a capsulo-ligamentous dislocation or JA. The frequency of JA in primary SS has yet to be estimated in the literature, except for one rare description of deforming arthritis.[27] In addition to the 15 JA patients in the present study, we found one other patient with JA in our hospital records (not shown in the Results section): a woman diagnosed as having SS based on positive sicca syndrome and Schirmer's test, inflammation of the salivary glands, Rubin–Holt stage II change on sialography, and positive serum antinuclear antibodies and anti-SSA antibodies. Although lymphocytopenia and 1(+) urine protein manifested, renal biopsy revealed no abnormality in this patient. She was therefore diagnosed as having primary SS.

Bell[28] stated that clinical and serological features of elderly SLE are very similar to those of SS. As shown in Table 2, patients Nos. 9–15 fulfilled only three criteria of SLE without arthritis. Of these, only No. 12, No. 13, No. 14, and No. 15, for whom SS was evaluated in the present study, were diagnosed as having SS (Table 3). When arthritis in these four patients was assumed to be a manifestation of SS, they were diagnosed as having primary SS but not SLE. On the other hand, JA in patient No. 11 was clearly attributed to SLE because SS was ruled out (Table 3). Consequently, in some of our patients with JA, it was difficult to discriminate between SLE and primary SS.

In conclusion, Jaccoud's arthropathy in patients with SLE is associated with Sjögren's syndrome, elderly SLE, HLA-A11, and HLA-B61. These clinical features might be characteristic of patients with Jaccoud's arthropathy and SLE.

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