Jaccoud arthropathy in systemic lupus erythematosus: clinical and serological findings

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Summary

Objective: To study the prevalence of Jaccoud arthropathy (JA) in a sample of local systemic lupus erythematosus (SLE) patients and its clinical and serological associations. **Methods:** 308 SLE patients from a single university center for the last two years were interviewed and examined. The presence of JA was searched for according to the JA index. After this, charts were reviewed for clinical and serological profile. **Results:** The studied sample was composed by 94.5% females and 5.5% males with mean age of 38.08 ± 12.04 years and mean disease duration of 29.68 ± 11.63 years. A JA prevalence of 6.1% was found in this sample. There was a positive association of JA presence with arthritis complaints ($p = 0.001$) and a negative association with renal involvement ($p = 0.028$). Patients with JA had higher positivity for anti-dsDNA ($p = 0.022$). **Conclusion:** Despite the positive association of JA with arthritis and anti-dsDNA, there was a negative association with nephritis. This could suggest that JA patients belong with a SLE subset with a better prognosis.

Keywords: Lupus erythematosus, systemic; arthritis; glomerulonephritis.

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Introduction

Jaccoud arthropathy (JA) is a non-erosive deforming type of arthropathy first identified in patients with rheumatic fever in the 19th century by Dr. Jaccoud[1], a French clinician. Later, it was also described in systemic lupus erythematosus (SLE) patients and in other diseases such as acquired immunodeficiency syndrome (AIDS), systemic sclerosis, dermatomyositis, hypocomplementemic vasculites, and necrotizing vasculitides[1-4]. This form of arthropathy causes severe deformities mainly in the hand joints with multiple subluxations; "swan neck" and "boutonniere" deformities in the fingers; "Z" distortion of thumbs; and ulnar drift of metacarpal-phalangeal joints, which can be easily misdiagnosed as rheumatoid arthritis[5]. Although most descriptions have focused on the hands, JA appears to be a generalized process that involves all capsular and periarticular tissues[6]. Unlike rheumatoid arthritis, all deformities in JA are reducible and usually cause little or no pain[6]. Joint function is rather well-preserved, and radiographic studies do not show evidence of bone or cartilage damage. In rheumatoid arthritis, the loss of stability is due to hyperthrophic synovitis; in JA, the process involves mainly periarticular tissue and ligaments[6]. Although articular involvement is one of the most common findings in lupus patients and frequently one of its initial manifestations[7], JA is described in only 2% to 35% of cases[8,9]. SLE is a disease with a wide array of signs, symptoms, and autoantibody profile. It appears that some patients develop a particular subtype of disease where a cluster of clinical and serological findings are found, which can be useful in predicting the complete clinical picture. In the present study the prevalence of JA in a sample of SLE patients from this service was analyzed, searching for associated clinical and serological findings.

Methods

This was an analytical and transversal study that was approved by the local committee of ethics in research, and all the participants signed an informed consent. All patients included fulfilled at least four of the classification criteria from the American College of Rheumatology (ACR) for SLE diagnosis[10]. The 308 included patients represented a sample of 74.7% of patients with SLE diagnosis attended to at this clinic from July 2009 to July 2011. They were included consecutively according to appointment order and willingness to participate in the study. Patients were interviewed and examined to determine the presence of JA, according to the JA index[9]. The JA index determines the number and degree of deformities in hand joints on a scale from 0 to 14. The JA diagnosis was established when the index was equal to or over five and hand radiology studies were normal. All patients with arthritis complaints were submitted to a radiological study of the affected joints to exclude the presence of erosions. Patients' charts were reviewed for presence of clinical findings that occurred during disease evolution and for serological profile. Clinical and autoantibody data were considered cumulatively and were obtained through chart review. Collected clinical data were considered as defined by the 1997 revised Classification Criteria of the ACR for SLE[10]. All patients with renal involvement (proteinuria over 500 mg on two or more occasions) were submitted to renal biopsy according to local protocol except those who presented with class VI disease. Neuropsychiatric manifestations were identified according to the American College of Rheumatology nomenclature and case definition for neuropsychiatric lupus[11]. Data on Raynaud phenomenon, myositis, arthralgia, sicca symptoms, and hypothyroidism were also collected. Raynaud phenomenon was defined by discoloration of fingers and/or toes induced by cold exposure or stress and observed by a doctor. Myositis was defined by proximal muscular weakness and rise in muscular enzymes in the absence of offending drugs or thyroid dysfunction; sicca symptoms were considered present if the patient had oral or ocular dryness not attributable to medications; arthralgia was characterized by joint pain without signs of inflammation. Hypothyroidism was considered present when TSH was above 4.0 mU/L on at least two occasions[12]. The autoantibodies considered for analysis were: anti-Ro/SS-A, anti-La/SS-B, anti-RNP, anti-Sm, anti-dsDNA, anticardiolipin (aCl) IgG, aCl IgM, LA (lupus anticoagulant), direct Coombs, and rheumatoid factor (RF). Anti-Ro/SS-A, anti-La/SS-B, anti-RNP, anti-Sm, aCl IgG, aCl IgM were tested by enzyme-linked immunoabsorbent assay (ELISA using ALKA and Orgentec Kits®); anti-dsDNA was tested by immunofluorescence technique (IFT) using *Crithidia luciliae* as a substrate. Lupus anticoagulant was examined through a screening test, the dilute Russell viper venom test (dRVVT) and confirmed by Russell Viper Venom Time Test (RVVT). IgM rheumatoid factor was examined by latex agglutination test (BioSystems®). Data was collected in contingency and frequency tables. Fisher's test and the chi-squared test were used for association studies of nominal data and unpaired *t*-test and Mann Whitney's test were used for numeric data. Variables with $p < 0.05$ in the univariate analysis were submitted to analysis through a model of logistic regression to determinate the odds ratio (OR) and 95% confidence interval. Calculation was performed with help of the software Graph Pad Prism version 4.0 and Medcalc version 12.1.3.0. The adopted significance level was of 5%.

Results

Description of the studied sample

In the 308 SLE studied patients, the mean age was 38.08 ± 12.04 years (from 14 to 76 years) with median disease duration of 87 months (from 1 to 468 months). The gender

distribution showed 291/308 (94.5%) females and 17/308 (5.5%) males. The mean age at diagnosis was 29.68 ± 11.63 years (5 to 69 years). In this sample, 76.9% of the patients were using antimalarial drugs; 12.9%, methotrexate; 2.59%, cyclophosphamide; 4.22%, mophetil mycophenolate; 15.58%, azathioprine; and 22.7%, steroids. The prevalence of clinical findings is seen in Table 1.

Table 1 – Cumulative prevalence of clinical findings in 308 systemic lupus erythematosus patients

	Number	Percentage
Photosensitivity	235/308	76.29%
Malar rash	153/298	51.34%
Discoid lesions	40/299	13.37%
Oral ulcers	134/298	44.96%
Raynaud phenomena	141/293	48.12%
Arthritis	189/305	61.96%
Migratory	n = 59	19.34%
Additive	n = 130	42.62%
Arthralgia	47/305	15.40%
Myositis	10/308	3.24%
Pleural effusion	50/307	16.28%
Pericarditis	34/305	11.14%
Renal involvement[a]	122/299	40.8%
Class 6	n = 13	4.34%
Class 5	n = 25	8.36%
Class 4	n = 45	15.05%
Class 3	n = 24	8.02%
Class 2	n = 15	5.01%
Leukopenia[b]	91/303	30.03%
Lymphopenia[c]	47/296	15.87%
Hemolytic anemia	21/300	7.00%
Plaquetopenia[d]	70/305	22.95%
Psychosis[e]	23/307	7.49%
Convulsions[e]	32/308	10.38%
Hipothyroidism	59/ 287	20.55%
Sicca symptoms	66/288	22.91%

[a]All proven by biopsy, except those in class 6; classification according to ISN/RPS 2004[12]; [b]Less than 4000/mm^3 on at least two occasions, without use of immunosupressive drugs; [c]Less than 1500/mm^3 on at least two occasions, without use of immunosupressive drugs; [d]Less than 100.000/mm^3 on at least two occasions, without use of immunosupressive drugs; [e]Identified according to the American College of Rheumatology's nomenclature and case definition for neuropsychiatric lupus[11].

In the studied population, 6.1% (19/308) of patients met the criteria for JA.

The serological profile of the studied sample showed that 130/300 (33.3%) had anti-dsDNA; 112/308 (36.3%) had anti-Ro; 55/290 (18.9%) had anti-La; 70/254 (27.4%) had anti-RNP; 64/292 (21.9%) had anti-Sm; 58/301 (19.2%) had aCl IgG; 46/254 (18.1%) had aCl IgM; 40/275 (14.5%) had a lupus anticoagulant; and 68/283 (24.02%) had rheumatoid factor.

Analysis of SLE population with JA in comparison to those without JA

The study of the demographic data in relation to the presence of JA demonstrated that there were no differences in age, gender, or age at diagnosis. The median disease duration in those with JA was 84 months, and in those without it was 120 months (p = 0.08). Analysis of clinical data according to the presence of JA showed that there was a significant statistical difference in arthritis (present in 94.7% of JA patients *versus* 59.7% in those without it; p = 001) and kidney involvement (present in 15.78% of JA patients versus 59.7% in those without it; p = 0.028). All other clinical variables, such as gender, median age, age at diagnosis, photosensitivity, malar rash, discoid lesions, oral ulcers, Raynaud phenomenon, arthralgia, myositis, pleural effusion, pericarditis, psychosis, convulsions, hematologic disorders, hypothyroidism, and sicca symptoms were equally distributed (p = ns). The serological profile in patients with and without JA demonstrated a statistically significant difference in anti-dsDNA antibodies prevalence, as can be seen in Table 2.

Table 2 – Comparison of serological data in 308 systemic lupus erythematosus patients according to the presence of Jaccoud arthropathy

	With JA n = 19	Without JA n = 289
Anti-dsDNA	13/19 - 68.4%	117/281 - 41.6%
Anti-Ro	8/19 - 42.1%	104/279 - 37.27%
Anti-La	2/18 - 11.1%	53/272 - 19.48%
Anti-Sm	5/18 - 27.7%	59/274 - 21.53%
Anti-RNP	5/17 - 29.4%	65/237 - 27.42%
aCl IgG	6/18 - 33.33%	52/283 - 18.37%
aCl IgM	3/15 - 20%	42/239 - 17.57%
LA	5/19 - 26.31%	35/256 - 13.67%
Coombs	0/17	17/238 - 7.14%
Rheumatoid factor	7/19 - 36.84%	61/264 - 23.10%

aCl, anticardiolipin; LA, lupus anticoagulant; JA, Jaccoud arthropathy; DNA, deoxyribonucleic acid.

All variables with p < 0.05 (renal disease, arthritis, and anti-dsDNA) were submitted to a logistic regression using Jaccoud arthropathy as the dependent variable. Arthritis and anti-dsDNA were found to influence the presence of Jaccoud arthropathy positively and renal disease negatively. An OR = 10.06 (95% CI; 1.30-77.36) was found for

arthritis; an OR = 2.93 (95% CI; 1.05-8.22) was found for anti-dsDNA, and an OR = 0.22 (95% CI;0.06-0.81) was found for renal disease.

Discussion

The pathogenetic factor that may cause certain SLE patients to develop JA is not yet clear. Some authors have associated JA with joint hypermobility, and others with hyperparathyroidism or with antiphospholipid syndrome[6,7]. van Vugt et al.[6] found a relationship of JA and antiphospholipid antibodies and suggested that small vessel thrombosis could cause ischemia and periarticular fibrosis. The study of the presence of joint hypermobility has controversial results[6,13,14]. Hyperparathyroidism secondary to renal failure was considered a potential factor as it causes tendinous laxity[13]. Another group of authors has linked JA to a persistent local inflammation[9,14]. Bywaters[15] proposed that constant joint inflammation in the synovial membrane and capsule causes fibrosis and capsule retraction, resulting in deformities. Although they are common, inflammatory reaction of joints in SLE are usually mild and transient. They tend to have more symptoms than objective signs, although some patients may have a more persistent process. Spronk et al.[9] found an association of JA with increased concentrations of C-reactive protein and suggested that this could be due to a persistent inflammatory reaction. According to these authors, infiltration of inflammatory cells in the articular tissues results in production of interleukin (IL)-1 and IL-6, which may induce an acute phase reaction. A study with magnetic resonance imaging detected capsular swelling and severe edematous tenosynovitis in lupus patients with JA[16]. In the present study, arthritis complaints were more common in patients who developed JA, which favors this hypothesis. The present sample had a high prevalence of renal disease, as expected in a tertiary center. An interesting outcome of the present study was the negative relationship of JA with renal involvement, despite a positive association with anti-dsDNA. Although this may seem paradoxical, since this autoantibody has been considered a marker of renal disease[12], the finding of a positive association with anti-dsDNA was also observed in two other studies[8,17]. Neither study noted any difference in the prevalence of renal involvement in patients with or without JA. Conversely, a study by van Vugt et al.[6] and another by Molina et al.[18] detected a negative relationship of JA with lupus nephritis, as the present study did. It should also be noted that in the present sample, all classes of renal involvement were present, and that the prevalence of positive anti-DNA may vary among them. As nephritis is a cause of high morbidity and even mortality in lupus patients, the presence of JA could indicate a subgroup of lupus patients with better prognosis. Another controversial point in the literature concerns disease duration in patients with JA. While some authors have found that JA is more common in lupus patients with longer disease duration[6,8], others such as Alarcón-Segovia et al.[17], found that JA is more frequent in those with shorter duration. In the present study there was no difference in disease duration, but a trend towards a shorter disease in lupus patients with JA was noticed. In conclusion, in the studied sample JA was associated with clinically detected arthritis, with more anti-dsDNA and with less renal involvement.

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