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Jaccoud's arthropathy in SLE: findings from a Latin American multiethnic population

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ABSTRACT

Objective To compare the clinical, laboratory and outcome features of SLE patients with and without Jaccoud's arthropathy (JA) from the *Grupo Latino Americano De Estudio del Lupus* (GLADEL) cohort.

Methods 1480 patients with SLE [(34 centres, 9 Latin American countries with a recent diagnosis (≤2 years)] constitute the GLADEL cohort. JA was defined as reducible deformity of the metacarpophalangeal axis, without radiographic erosions at any time. Within this cohort, a nested case–control study was carried out. Control was matched for age, gender and centre in a 1:3 proportion. The variables included were: sociodemographic, clinical and immunological features, disease activity, damage and mortality. Comparisons were performed with Wilcoxon and χ^2 tests for continuous and categorical variables, respectively. ORs and 95% CIs and Kaplan-Meier survival curve were estimated.

Results Of 1480 patients, 17 (1.1%) JA patients were identified; 16 (94.1%) of them were women, mean age: 31.0 years (SD 12.0). Five (29.4%) patients presented JA at SLE diagnosis and 12 (70.6%) after. The median follow-up time and all disease features were comparable in both groups except for a higher frequency of pneumonitis in the patients with JA [4 (23.5) vs 1 (2.0); p=0.012; (OR: 15.4; 95% CI 1.6 to 149.6)]. The SLE disease activity index, Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage Index and the Kaplan-Meier survival curve were similar in both groups.

Conclusion JA may tend to appear early in the course of SLE; it seems not to have an impact on disease activity, damage accrual or in survival.

INTRODUCTION

Classically, Jaccoud's arthropathy (JA) is defined as a reversible, non-erosive, deforming arthropathy; it was originally described in patients with rheumatic fever, but since it has been described in patients with other diseases such as Sjögren's syndrome, scleroderma, vasculitis, psoriatic arthritis, dermatomyositis, ankylosing spondylitis, mixed connective tissue disease and especially in SLE.[1 2] Moreover, this arthropathy has been associated with other non-rheumatic diseases.[3]

The prevalence of JA in SLE varies between 2% and 5% according to the published series.[1–4] It affects mainly the hand joints but may affect the feet or other joints. Its aetiology has not been clarified, but it has been associated with clinical and laboratory manifestations, such as cardiac involvement, sicca syndrome and antiphospholipid antibody positivity.[5 6] Likewise, JA negatively affects the quality of life of affected patients.[7]

Studies on JA are very scarce in the literature; for the most part, they are limited to a few case series. Data from a Latin American cohort will certainly help to improve our understanding of this rare condition, which can lead to a loss of joint function as well as poor quality of life.

The aim of this study was to compare the clinical, laboratory and outcomes features in patients with JA and without JA, from the *Grupo Latino Americano De Estudio del Lupus* (GLADEL) cohort.

METHODS

GLADEL was established as a longitudinal multiethnic inception cohort of Latin American patients with SLE with up to 2 years of disease duration from diagnosis. Participants' enrolment and data collection started in 1997 following a established common protocol in 34 centres distributed among nine Latin American countries.

Researchers at all centres were training in data collection prior to study initiation.

All researchers followed local regulations according to their institutional review boards. Although the diagnosis was made based on clinical and laboratory features, and according to the expertise of the investigators,

fulfilment of four of the 1982 American College of Rheumatology (ACR) SLE classification criteria at the time of diagnosis was not mandatory.

For the current study, patients who presented JA at any time in the course of the disease were selected as cases; being this a nested case–control within a cohort, matching was performed for age, gender and centre in a 1:3 proportion. JA was defined as a reducible deformity of the metacarpophalangeal axis, in the absence of radiographic erosions.

The variables examined were: sociodemographic, cumulative clinical and immunological features (from disease onset to the last visit). In addition, the following variables were included: the average disease activity over the course of SLE as assessed with the SLE Disease Activity Index (SLEDAI); damage accrual at the last visit assessed with the Systemic Lupus International Collaborating Clinics/ACR damage Index (SDI), excluding JA; and mortality.

Statistical analysis

Categorical variables were summarised as frequencies and percentages, while continuous variables are presented as medians with their IQRs. Comparisons between the two groups were performed with the Wilcoxon and χ^2 tests for continuous and categorical variables, respectively. ORs and 95% CIs were estimated. The Kaplan-Meier survival curve was estimated, and the log-rank test was calculated.

Statistical significance was set at p≤0.05. All analyses were performed using the SAS software, V.9.4.

RESULTS

A total of 1480 patients with SLE were included in the GLADEL cohort. Seventeen (1.1%) developed JA. Sixteen (94.1%) were women, with a mean age of 31.0 years (SD 12.0). The three major cohort's ethnic groups were represented: 10 (58.8%) Caucasian, 5 (29.4%) Mestizo and 2 (11.8%) Afro-Latin American.

A total of five (29.4%) patients presented JA at the time of SLE diagnosis and 12 (70.6%) during their follow-up. The median follow-up time in the two patient groups was similar [69.0 months (IQR 12.0), vs 57.0 (IQR 37.0); p=0.720].

Table 1 describes and compares the sociodemographic characteristics, cumulative clinical and serological features, median SLEDAI and SDI between patients with JA and the control group. Within the clinical features, patients with JA had pneumonitis more frequently that the control patients [4 (23.5) vs 1 (2.0); p=0.012; (OR: 15.4; 95% CI 1.6 to 149.6)], but all other variables examined were comparable in both groups. Likewise, the Kaplan-Meier survival curve was similar in the both patient groups (p=0.463) (data not shown).

DISCUSSION

The prevalence of JA in this cohort was low (1.1%) when compared with the frequencies reported in other studies[1 2 4] where the ranges varied between 2% and 5%. This could be due to the recent diagnosis of SLE and to the relatively short follow-up time of the members of this cohort. The majority of the authors agree that JA is a relatively late SLE manifestation, although other authors propose that JA could be an early disease manifestation.[4 8] The dissimilar frequencies observed in the studies alluded to may relate to inclusion bias[1–4 9] and the definition of JA used by different authors. In fact, a clear-cut definition of deforming arthropathy in SLE has not been well accepted or developed; the classification criteria can be clinical (any deviation of the metacarpal finger axes assessed by a goniometer), as described by Alarcón-Segovia *et al*[4] or using the diagnostic index developed by Spronk *et al*,[8] which allows for the presence of different deformities, and attributing JA a score of over 5 points; however, van Vugt *et al*[2] added the presence of erosions in hand and feet radiographs. Thus, patients may have an erosive arthropathy (EA), which several authors have called it Rhupus[2 8] or, in the absence of erosions on hand radiographs, definitive JA or mild deforming arthropathy (MDA), depending on the score values.

The aetiopathogenesis of JA is not at all clear; several theories have been postulated: hypermobility of the joints, hyperparathyroidism secondary to renal failure, in advanced stages of the disease, and consequently tendinous laxity, as well as the persistence of mild joint inflammation.[1 2 10]

Many authors claim that persistent inflammation and small erosions may be under diagnosed on radiographs but can be detected on ultrasound (US) or on MRI.[11–13] Sá Ribeiro *et al*[13] studied 20 patients with SLE with JA and more than 300 joints were evaluated by MRI. Synovitis was observed in 67.3%, tenosynovitis in 38.5% and in 5.3% in small areas of erosions. Similarly, Lins *et al*[14] examined 40 patients and 560 joints by US; 47.5% had synovial hypertrophy, 22.5% had tenosynovitis and 5.0% small erosions; there was no association between these findings and disease activity (p=0.33).

Within the clinical features, lupus pneumonitis was found more frequently among the patients with JA than those without it; however, the CI was wide, and thus, this finding needs to be interpreted with caution. We did not find a higher frequency of renal manifestation among our patients with JA. Van Vugt *et al*[2] described a negative association between the presence of JA and lupus nephritis. This apparent protective effect could not be corroborated by Lhakum *et al*[15]; they studied 458 patients with SLE; deforming arthropathy was present in 40 of them (8.7%). The prevalence of EA, JA and MDA was 2.8%, 1.8% and 4.1%, respectively. In this study, a higher occurrence of renal involvement (69.2%) as well as another major organ involvement, particularly neurological and haematological, was found among the patients with JA.

We found no specific relationship between JA and any autoantibodies including anti-SSA/Ro, SSB/La and antiphospholipid antibodies. These last have even been postulated as part of pathophysiology, with microvascular

Table 1 Characteristics of patients with JA and controls from GLADEL cohort

Variables	JA (n=17)	Control (n=51)	P value	OR (95% CI)
Age at diagnosis, years (median, IQR)	31.0 (12.0)	29.0 (14.0)	0.590	
Follow-up in the cohort, months (median, IQR)	69.0 (21.0)	57.0 (37.0)	0.720	
Female gender (n, %)	16 (94.1)	48 (94.1)	1.000	
Ethnic group (n, %)				
Caucasian	10(58.8)	36(70.6)	0.665†	
Mestizo	5(29.4)	11(21.5)		
Afro-Latin American	2(11.8)	3(5.9)		
Others	0(0.0)	1(2.0)		
Residence (n, %)				
Urban	17 (100.0)	48 (94.1)	0.567	
Socioeconomic status (n, %)				
High/high–middle	3 (17.6)	8 (15.7)	0.586	
Middle	5 (29.4)	12 (23.5)		
Middle–low/low	9 (52.9)	31 (60.8)		
Education level; years (n, %)				
0–7	7 (41.2)	19 (37.3)	0.570	
8–12	9 (52.9)	24 (47.1)		
>12	1 (5.9)	8 (15.7)		
Type of social health coverage (n, %)				
Public	14 (82.4)	40 (78.4)	0.999	
Private	3 (17.6)	11 (21.6)		
Cumulative clinical features, (n, %)				
Malar rash	11 (64.7)	33 (64.7)	1.000	
Discoid lupus	1 (5.9)	5 (9.8)	0.999	
Photosensitivity	11 (64.7)	31 (60.8)	0.773	
Oral ulcers	9 (52.9)	24 (47.1)	0.674	
Arthritis	16 (94.1)	43 (84.3)	0.432	
Pleuritis	4 (23.5)	8 (15.7)	0.477	
Pericarditis	3 (17.6)	8 (15.7)	0.999	
Neurological disorder	8 (47.1)	17 (33.3)	0.309	
Renal disorder	7 (41.2)	30 (58.8)	0.205	
Haematological disorder	13 (76.5)	42 (82.3)	0.723	
Immunological disorder*[10]	11 (84.6)	40 (88.9)	0.647	
ANA	16 (94.1)	49 (96.1)	0.999	
Autoantibodies, (n,%)				
Anti-dsDNA	6 (35.3)	32 (62.7)	0.088	
Anti-SSA/Ro	5 (29.4)	14 (27.4)	0.999	
Anti-SSB/La	3 (17.6)	6 (11.8)	0.680	
Antiphospholipid	11 (64.7)	25 (49.0)	0.261	
Hypocomplementaemia	12 (70.6)	33 (64.7)	0.657	
Raynaud's phenomenon	9 (52.9)	25 (49.0)	0.779	
Xerophthalmia and xerostomia	6 (35.3)	9 (17.6)	0.176	
Lupus pneumonitis	4 (23.5)	1 (2.0)	0.012	15.4 (1.6–149.6)
SLEDAI average at follow-up (median, IQR)*[14]	3.83 (4.29)	3.33 (5.31)	0.606	
SDI score (last visit) (median, IQR)	2 (4)	1 (3)	0.647	
Mortality at follow-up, (n,%)	4 (23.5)	7 (13.7)	0.447	

*Missing data.
†To calculate the p value, the categories African, Latin American and others were combined.
ACR, American College of Rheumatology; GLADEL, Grupo Latino Americano De Estudio del Lupus ; JA, Jaccoud's arthropathy; SDI, SLICC/ACR Damage Index; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC, Systemic Lupus International Collaborating Clinics.

damage.[4 5] Likewise, JA does not appear to have a direct impact on either disease activity, damage accrual or survival in our cohort.

Our study has some limitations. First, the small number of individuals identified precludes us from making definitive conclusions about our findings; second, although investigators participating in the GLADEL cohort were trained in data collection prior to study initiation, it is possible that JA may have not been detected by some of them; furthermore, the lack of more refined methods to evaluate erosions makes it possible that some patients may have been misclassified; third, data on rheumatoid factor and anticyclic citrullinated peptide, as well as, acute phase reactants and auto antibodies were not systematically obtained in our patients; and fourth, the association between JA and pneumonitis needs to be interpreted with caution given its wide CI.

Despite these limitations, we can conclude that JA could be considered a manifestation that may appear early in the course of SLE and associated with certain clinical features (pulmonary involvement) but apparently has no impact on either disease activity, damage accrual or survival.

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