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LETTER

Characteristics of Sjögren's syndrome associated with rheumatoid arthritis

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Sjögren Syndrome (SS) classically associates sicca syndrome, pain and asthenia. Systemic manifestations may develop with potentially severe organ damage including pulmonary, neurological, renal involvement and lymphoma.[1 2] SS can be associated with rheumatoid arthritis (RA). Despite this frequent association, few studies have investigated differences between primary Sjögren syndrome (pSS) and SS associated with RA(SS/RA).[3 4]

We have conducted a retrospective single-centre case-controls study. Patients were identified in the Paris-Saclay cohort, a prospectively collected database. Cases were patients fulfilling both ACR/EULAR 2016 criteria for SS and ACR 2010 criteria for RA and followed between 2000 and 2019. For each case, two controls from our local pSS cohort were randomly assigned and matched on disease duration. Disease activity was assessed using the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI)[5] and ESSDAI cumulative score (Cumulative ESSDAI). The latter was calculated considering for each domain, the highest value reached by the patient during his/her follow-up. SS/RA and pSS patients were compared using a Chi-square test for non-normal binary variables and Mann-Whitney-Wilcoxon test for non-normal numeric variables. The p was retained as significant in the statistical analyses if <0.05.

Sixty-two SS/RA patients were compared with 124 pSS patients (table 1). There were more women among the pSS group (p=0.03). We observed a higher disease activity in the SS/RA group when considering ESSDAI and cumulative ESSDAI. We also performed analyses excluding joint involvement: there was no more difference between the two groups, which reflects the weight of the articular domain in the activity of the disease in the SS/RA group. There was higher prevalence of arthralgia and arthritis in the SS/RA group. Pulmonary involvement was also significantly more frequent in SS/RA group; 9/62 (14.5%) patients (six interstitial lung disease (ILD): 4 non-specific interstitial pneumonia (NSIP) and two non-specific ILD), 1 bronchiectasis, 1 bronchial disorder and one pulmonary cysts) were compared with 7/123 (5.7%) patients in the pSS group (3 ILD: 2 NSIP and one non-specific ILD, 3 bronchiectasis and one obstructive bronchial disorder). pSS patients presented more skin or vaginal dryness and parotid gland enlargement. We found higher ESR levels and higher rate of RF positivity in the SS/RA group compared with pSS. Even though numerically higher in the pSS group, the frequency of lymphoma did not significantly differ between groups (p=0.267). There was no difference between the two groups on the other parameters.

Our study confirms previous reports showing that pSS patients have more frequently parotid gland enlargement.[4 6] As described by He *et al*, we found that patients with SS/RA have more frequently articular and pulmonary involvement.[4] It is difficult to decipher if articular involvement was linked to RA or to SS in these patients. Of note, in our study, more than 50% of the RA/SS patients had erosions. Regarding lung involvement, discrimination between SS linked or RA linked manifestations is also challenging. ILD complicating pSS tends to give more NSIP while ILD complicating RA tends to give usual interstitial pneumonia (UIP). In our study, pulmonary involvement seemed to be mainly due to SS in the SS/RA group since there was no UIP.

This study shows that patients with pSS and SS/RA have the same level of systemic disease activity. Thus, in RA patients, sicca symptoms should not be neglected and should be

Table 1 Comparison of pSS and SS/RA

	pSS	SS/RA	P value
Number of patients	124	62	
Female sex (n,%)	112/124 (90%)	49/62 (79%)	0.033
Age	55.06(13,9)	53.55(14,3)	0.539
Disease duration	8.8 years(8.8)	8.1 years (8.8)	
Tobacco	19/112 (17%)	16/55 (29%)	0.07
Asthenia (n, %)	99/122 (81%)	35/41 (85%)	0.541
Dry eye (n, %)	107/124 (86%)	47/56 (84%)	0.676
Dry mouth (n, %)	111/124 (89%)	48/55 (87%)	0.660
Others sicca syndrome (vagina and skin) (n, %)	90/118 (76%)	30/51 (58%)	0.022
Parotid enlargement (n, %)	61/123 (49.6%)	13/59 (22%)	<0001
Myositis (n, %)	1/123 (1%)	1/60 (2%)	0.602
Arthralgia (n, %)	61/108 (56.5%)	54/62 (87%)	<0001
Arthritis (n, %)	20/123 (16.3%)	57/62 (92%)	<0001
Peripheral neurological involvement (n, %)	10/121 (8.3%)	1/62 (1.6%)	0.073
Central neurological involvement (n, %)	2/123 (1.6%)	0/62 (0%)	0.313
Pulmonary involvement (n, %)	7/123 (5.7%)	9/62 (14.5%)	0.044
Renal involvement (n, %)	3/123 (2.4%)	0/61 (0%)	0.219
Lymphadenopathy, (n, %)	15/123 (12.2%)	7/62 (11.3%)	0.858
Lymphoma (n, %)	9/123 (7%)	2/62 (3%)	0.267
IgG levels (g/L)(Mean (SD))	13.6 (6.6)/113	15 (4.7)/45	0.067
Presence of monoclonal peak (n, %)	10/114 (9%)	7/55 (13%)	0.423
CRP (mg/L)(Mean (SD))	6.3 (6.5)/112	13.6 (23.4)/61	0.184
ESR (mm at 1 hour)(Mean (SD))	23.6 (21)/109	39.7 (27.3)/58	<0001
Lymphocytes count (/mm^3)(Mean (SD))	1673 (1212)/118	1657(636)/62	0.494
Beta2-microglobulin (mg/L)(Mean (SD))	2.3 (1.1)/101	2.7 (1.5)/39	0.172
LDH (U/L)(Mean (SD))	344 (101)/105	350 (57.9)/37	0.344
C3 (g/L)(Mean (SD))	1.09 (0.3)/111	1.1 (0.3)/43	0.893
C4 (g/L)(Mean (SD))	0.31 (0.9)/111	0.22 (0.1)/42	0.987
Anti-SSA antibodies (n, %)	86/120 (72%)	35/60 (58%)	0.072
Anti-SSB antibodies (n, %)	48/122 (39%)	17/58 (29%)	0.19
RF positivity (n, %)	57/119 (48%)	54/62 (87%)	<0001
RF levels when detectable (UI/mL)(Mean (SD))	426(794)	348(569)	0.651
Anti-CCP (n, %)	1/107 (1%)	55/62 (89%)	<0001
Cryoglobulinemia (n, %)	2/123 (2%)	3/62 (5%)	0.203
ESSDAI	3.74[5]	6.3 (5.5)	<0001
Cumulative ESSDAI	6.8 (7,5)	9.2 (5.7)	<0001
ESSDAI without joint domain	2.85 (4.8)	3.2 (4.8)	0.971
Cumulative ESSDAI without joint domain	5.4 (7.4)	4.5 (5.3)	0.573

Variables are presented as mean (SD) or number and percentage.

explored in order to detect an associated SS and to adapt the follow-up accordingly especially concerning pulmonary involvement and risk of lymphoma.

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