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SLE, Sjögren's and APS - clinical aspects (other than treatment)

SAT0262 BCL2-ASSOCIATED ATHANOGENE 3 PROTEIN IS ASSOCIATED WITH B-CELL HYPERACTIVITY INCLUDING LYMPHOMA IN PRIMARY SJÖGREN'S SYNDROME

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Background: Bcl2-associated athanogene 3 (BAG-3) is a co-chaperone protein that interacts with the ATPase domain on heat-shock protein 70. BAG-3 is involved is several biologic processes including apoptosis, cytoskeleton organization and autophagy and, therefore, it has been extensively investigated in the field of tumorigenesis (1). In particular, BAG-3 expression is constitutive in human primary tumors including leukemias and lymphomas and it is induced in different normal cell types, including leukocytes, by a variety of stimuli. BAG-3 is able to induce and maintain cell proliferation, resistance to therapy and cell motility, namely metastatization. On this basis, a role of BAG-3 in chronic inflammatory diseases may be postulated, but data on this topic are not available.
Objectives: The purpose of our study was to investigate the expression of BAG-3 in primary Sjogren's syndrome (pSS) and the relationship with clinical and serological features.
Methods: BAG-3 concentration was assessed in the serum of 103 patients with pSS according to the 2002 American-European classification criteria and in 40 sex and age matched healthy donors (HD). Clinical and serological records were collected and statistical analysis was performed with SPSS 21.0.
Results: Twenty-six pSS patients were positive for BAG-3 (BAG-3+), with serum levels ranging from 32.1 to 950 pg/ml. When setting the cut-off value according to the highest value found in HD (300 pg/ml), we identified 13 pSS patients displaying a peculiar clinical serological phenotype. In detail, in this subgroup of pSS patients the prevalence of purpura, low C4, both anti-Ro and anti-La autontibodies, rheumatoid factor and lymphoma was higher, when compared to pSS patients with BAG-3 levels $<$300 pg/ml or BAG-3- (all $p<0.05$). Furthermore, they displayed less frequently sicca symptoms such as xerostomia and xerophtalmia (both $p<0.05$). Binary logistic regression analysis revealed that pSS patients with BAG-3 levels $>$300 pg/ml had on odds ratio (OR) of 12 (95% CI 1.9–86, p=0.009) for lymphoma and this association was independent of the presence of purpura, a well know marker of lymphoma in pSS. When including low complement, another feature associated with lymphoma, in the multivariable analysis, both low C4 and BAG-3 levels $>$300 pg/ml resulted independently associated to lymphoma (OR=24 and 12.4 respectively).
Conclusions: Our study assessed for the first time serum BAG-3 levels in a large cohort of pSS patients. The results showed that the highest levels of BAG-3 identify a peculiar clinical and serological pSS phenotype, as consequence of a B-cell hyperactivity. Since it is known that BAG-3 is an anti-apoptotic protein playing a pivotal role in cell survival, and that B-cell hyperactivity in pSS is the consequence of coordinated and integrated actions of several stimuli and appropriate cytokines, our results may suggest that BAG-3 overexpression is involved in B-cell proliferation and activity, as well as in oligoclonal and monoclonal expansion in pSS.
References:
[1] Rosati A et al. Cell Death Dis 2011;2:e141.
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SAT0263 NEOPLASIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SPAIN: RELESSER REGISTRY DATA

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Background: There is limited evidence on the risk of neoplasia in autoimmune diseases such as systemic lupus erythematosus.
Objectives: The objective of this study is to analyze the incidence of cancer in the Spanish population with SLE and the factors associated in its development: RelesSER Registry Data.
Methods: We calculated the incidence density of malignant neoplasms, the standardized incidence ratio and the average time to develop the first neoplasm after diagnosis of SLE in patients of the SLE registry of the Spanish Rheumatology Society (RelesSER) fulfilling ACR97 criteria. We carried out a bivariate analysis of the associated factors to neoplasms and multivariate by logistic regression.
Results: A total of 3607 patients (90.4% female) were included. We registered 140 neoplasms in women (4.3%) and 14 in men (4%) ($p<0.821$). Incidence density 7.3/1000 patient-years (95% CI:4.85–10.98) (7.39 in patient-years women and 6.93 in men) without significant differences. After stratification by gender and age, cancer appeared in 3.2% of the women aged under 45 versus 3.8% of the men; 4.1% of women aged 45–65 years versus 5.9% of men and a 5.3% of women 65 and older versus 2.5% of men the same age. The standardized incidence ratio (SIR) was 2.16; 1.51 in men and 2.38 in women, highest for women under 65 years old. The SIR for $>$65 years was 0.98; 0.59 in men and 1.55 in women.
The average time until de development of the first malignant neoplasm was 10 years (RI:5.75–17.00), being lower in women [9.5 (RI: 5.00–17.0) years] than in men [12.5 (8.75–17.5)] and in patients under 45 years versus over 45 years [8.0 (RI: 5.00–16.00)].
Malignant neoplasms were the cause of death in 10% of the patients (15/154), predominantly hematological and breast cancers, both at 19% followed by lung cancer in 14.3%.
Factors associated to malignant neoplasms in the bivariate analysis are shown in (table 1). No immunosuppressive therapy was associated with the development of neoplasms. In the multivariate model, adjusted for age and time of disease duration, age was the only significant variable (OR:1.030; 95% CI: 1.003–1.059; p=0.029) with a trend for ACE inhibitors use (OR:1.866; 95% CI: 0.808–4.306; p=0.144), SLEDAI (last visit) (OR: 0.904; 95% CI: 0.806–1.015; p=0.089, SLICC/ACR DI) (without neoplasias) (OR: 1.160; 95% CI: 0.961- 1.401; p=0.123), and duration of the disease in months (OR: 1.003; 95% CI: 1.000–1.006; p=0.068).

Table 1

	Cáncer	Control	*p*
Gender, men %	4	96	0.821
Gender, women %	4.3	95.7	0.821
Mean age at first criterion, years (DS)	38.35 (16.01)	32.72(14.29)	<0.001
Diagnostic age SLE, years (DS)	40.37 (15.68)	34.75 (14.46)	<0.001
Age at last evaluation, years, mean (DS)	57.74 (14.38)	46.17 (14.58)	<0.001
Disease duration (months), mean (DS)	208.71 (102.95)	140.1 (99.69)	<0.001
Follow-up in Rheumatology (months), mean (DS)	170. 1 (90.75)	118.12 (86.90)	<0.001
Sjogren´s syndrome, %	20.5	14.1	0.029
SLEDAI, median [p25-p75]	1.00 [0.00-3.25]	2.0 [0.00-4.00]	0.026
KATZ, median [p25-p75]	3 [2-4]	2 [1-3]	0.001
SLICC*, median [p25-p75]	1.00 [0.00-3.00]	0.00 [0.00-1.00]	<0.001
CHARLSON*, median [p25-p75]	3 [2.00-4.00]	1 [1.00-3.00]	<0.001
Time on antimalarals (months) median [p25-p75]	78.00 (27.75-136.50)	60.00 (24.00-119.00)	0.099

Conclusions: The incidence of neoplasia in Spanish women with SLE is higher than expected for age and gender. Malignant neoplasms were the cause of death in 10% of the patients, predominating hematological and breast cancers followed by lung cancer.
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SAT0264 VALVULOPATHY AND PULMONARY HYPERTENSION IN A SERIES OF PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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Objectives: To evaluate the prevalence of cardiac valvular involvement and