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POS0289

CANCER RISK IN IMMUNOSUPPRESSED SCLERODERMA PATIENTS: A PROPENSITY SCORE MATCHING ANALYSIS

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Background: An increased incidence of cancer in patients with systemic sclerosis (SSc) is well-established¹. Current knowledge about the onco-transforming power of immunosuppressive treatments in both non-rheumatological and rheumatological pathologies, suggests an increased incidence of hematological and solid neoplasms². Evidences on the possible role of the immunosuppressants in the onset of cancer during SSc are lacking.

Objectives: To evaluate the incidence of malignancies in SSc patients exposed to immunosuppressive therapy.

Methods: The incidence of neoplasia in a cohort of 600 patients with SSc was evaluated retrospectively. Patients diagnosed with malignancy within 36 months from SSc onset were excluded from the analysis since suspected for paraneoplastic form. Patients exposed to methotrexate, cyclophosphamide, azathioprine and mycophenolate were confronted with a group comparable for age at onset, sex, disease variant, autoantibodies and exposure to other disease-specific therapies, using propensity score matching analysis. The considered follow-up was between the clinical onset and the diagnosis of cancer or the last available visit or the twenty-fifth year of illness.

Results: The analysis was carried out on 526 patients observed for an average period of 12.1 ± 6.0 years (males 9.5%, age at onset 49.0 ± 15.3 years); 24.9% had diffuse cutaneous variant of the disease and 39.0% and 34.8% were respectively positive for anti-centromere and anti-Scl70 antibodies. During the follow-up, 19.0% of patients were exposed to cyclophosphamide, 15.3% to azathioprine, 14.4% to methotrexate and 11.6% to mycophenolate mofetil. Sixty-five cancer diagnoses were made after the 36th month from onset (incidence 1.02: 100 patients/year), comprising 16 mammary cancers, 12 cancers of the gastro-intestinal tract, 11 cancers of the head-neck area, 10 cancers of the lungs, 9 cases of skin-cancer, 5 haematological malignancies and 1 brain tumour. The incidence of cancers did not differ in relation to treatment with cyclophosphamide ($X^2 = 0.001$, $p = 0.961$), azathioprine ($X^2 = 2.141$, $p = 0.143$), mycophenolate mofetil ($X^2 = 0.001$, $p = 0.993$) or methotrexate ($X^2 = 0.920$, $p = 0.337$) (Figure 1).

Conclusion: Our data are consistent with an increased incidence of neoplasms in the course of SSc, with a rate that appears almost doubled compared to the general Italian population with similar sex and age distribution (0.55: 100 patients/year; Italian

Association of Tumor Registries data³). In our SSc cohort this risk is independent of exposure to immunosuppressive drugs commonly used for the treatment of scleroderma disease.

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POS0290

PREDICTING RISK FACTORS OF MALT LYMPHOMA IN SJÖGREN'S SYNDROME

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Background: Primary Sjögren Syndrome (SS) is a slowly progressive systemic autoimmune disease complicated by lymphoma, with mucosa associated lymphoid tissue (MALT) type being the most common lymphoma form. Several predictors related to pSS associated lymphomas have been described, but there are no studies focusing on specific risk factors for the MALT histologic subtype.

Objectives: To identify predictors at SS diagnosis for MALT lymphoma development in pSS patients using simple clinical features.

Methods: From 815 SS patients of a single center fulfilling the 2016 ACR/EULAR criteria, those with subsequent development of MALT lymphoma according to the 2016 WHO classification were identified and matched in 1:2 ratio, with non-lymphoma SS control patients according to age, disease duration from SS diagnosis and gender. Lymphoma patients diagnosed within a year from SS diagnosis were excluded from the current study. Clinical, laboratory, histologic data as well as the ESSDAI scores at the time of SS diagnosis were recorded and compared between lymphoma and non-lymphoma patients. Independent lymphoma predictors were identified by a data driven Fast Correlation Based Feature selection (FCBF)/Logistic Regression (LR) algorithm.

Results: A unified dataset of 57 MALT lymphoma patients and 114 non lymphoma controls along with 39 features/variables was generated. The median age of SS diagnosis and the disease duration from SS diagnosis to lymphoma diagnosis (lymphoma group) or last follow up (control group) was 50,5 years old (range 25-77) and 7 years (range 0- 30) for the control group and 50 years old (range 24-70) and 8 years (range 1 -30) for the lymphoma group, respectively. MALT lymphoma patients presented more frequently with palpable purpura (23,2% vs 5,3% $p=0,001$), cryoglobulinemia (30,2% vs 1,6% $p<0,0001$), low C4 serum levels (62,9% vs 32,1% $p=0,0003$), rheumatoid factor (76,9% vs 56,1% $p=0,01$), anti La/SSB antibodies (33,9% vs 50,8% $p=0,049$) and higher median ESSDAI score (5 vs 2, $p<0,0001$). In contrast, autoimmune thyroiditis was more prevalent in controls (48,2% vs 18,6%, $p=0,004$). The FCBF/LR model revealed cryoglobulinemia ($p=0,03$) and ESSDAI at SS Diagnosis ($p<0,001$) as the only independent lymphoma predictors.

Conclusion: MALT is the predominant pSS related lymphoproliferative histologic type, associated with systemic disease activity and vasculitic manifestations at SS diagnosis. Cryoglobulinemia and ESSDAI score were proven independent risk factors for MALT lymphoma development.

Table 1. An FCBF-based multivariable logistic regression analysis results for investigating risk factors for MALT lymphoma development

Prominent feature	Regression coefficient	Odds ratio	p-value	CI low	CI upper
Cryoglobulinemia	1.67	5.342	0.033*	1.18	24.327
Total ESSDAI at diagnosis	0.28	1.318	<0.001*	1.208	1.439
Kidney involvement	0.07	1.069	0.5	0.101	0.351

* $p < 0.05$ (95% confidence interval). The rest of the features that participated in the analysis include the following: Palpable purpura, Low C4, Salivary gland enlargement, Lacrimal gland enlargement, ANA Titers, RF, Focus score at Sjögren diagnosis, PNS involvement, Anti-La, Disease duration from SS onset to SS diagnosis, Neutrophils<1500, Autoimmune thyroiditis, Lung involvement – interstitial disease Type, Lymphocytes<1000, Lymphadenopathy fixed, Arthralgias, Dry eyes, Raynaud, Gender, Age at Sjögren diagnosis, Dry mouth, Aca, Hb<12.5g/dL, ANA, Disease duration from SS Diagnosis to Lymphoma diagnosis or last follow up, Anti-Ro, Arthritis, WBC<4000/ μ L, Lung involvement bronchocentric disease, Interstitial renal disease, PLTs<100.000/ μ L, Liver involvement-PBC, Liver involvement–autoimmune hepatitis, CNS involvement. •AUC=0.78