p=0.01) when compared to patients with both abnormal SGUS findings and LGS focal lymphocytic sialadenitis.

Conclusion: SGUS and LSG histopathology showed only a moderate correlation in patients with pSS. SGUS may be useful to identify pSS patients with a more severe inflammatory LSG infiltrates, ultimately contributing to promote non-invasive phenotyping of multiple subsets in pSS.

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THU0260

SYSTEMIC LUPUS ERYTHEMATOSUS AND CYTOPENIAS: THE KEY FINDINGS IN BONE MARROW

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Background: Cytopenias are common in systemic lupus erythematosus (SLE), and it is fundamental to determine their etiology in order to establish an adequate therapeutic strategy.

Objectives: To describe the findings in the bone marrow aspirations (BMA) and biopsies of patients with SLE and cytopenias, as well as clinical and laboratory features associated with the etiology of the hematological abnormalities.

Methods: We performed a retrospective study in a third-level hospital in Mexico City. We included patients who fulfilled ACR criteria for SLE, presented with cytopenias and had a BMA and biopsy performed between 2000 and 2016. We described the main aspirate and biopsy findings, and also analyzed the final diagnosis and its association with clinical, laboratory and serological features.

Results: We included 101 patients; median age was 32 years and 81.2% were women. Leukopenia (<3000 cells/μl) was found in 47.5% of patients, with 29.7% having moderate or severe neutropenia (<1000 cells/μl). Lymphopenia (<1000 cells/μl) was a common finding (71.3% of patients). Moderate-to-severe thrombocytopenia (<50 K/μl) was present in 28.7% of patients. Finally, 25.8% of patients presented with pancytopenia. Regarding bone marrow findings, there was erythroid dysplasia in 50.5% of patients, granulocytic dysplasia in 28.7% and megakaryocytic dysplasia in 16%. Myelofibrosis was found in 2.6%. An increase in plasma cells (≥5%) was found in 21.8%.

In 72.3% of patients, bone marrow interpretation was conclusive. The most common diagnoses were disease activity (24.8%) and drug-associated myelotoxicity (28.7%). When compared to other etiologies, in patients with cytopenias secondary to disease activity, it was more frequent for the bone marrow be hypercellular (56 vs 23%, p=0.006) and to have increased megakaryocytes (40 vs 17.4%, p=0.048). Conversely, granulocytic dysplasia was less common in this group of patients (17.4% vs 54.3%, p=0.036).

We analyzed factors associated with both activity and toxicity as final diagnoses (Table 1). After multivariate analysis, a neutrophil count <1000 cells/μl was a protective factor for disease activity (OR 0.021; 95% CI 0.001-0.428, p 0.012). On the other hand, a history of renal activity (OR 4.3; 95% CI 1.3-14.2, p=0.024) and neutrophils less than 1000 cells/μl (OR 4.05; 95% CI 1.15-14.19, p=0.029) were found to be independent risk factors for myelotoxicity.

Table 1.

Characteristic	Disease activity (N=25)	Drug-associated toxicity (N=28)	p
History of disease activity	80%	86%	0.719
- Mucocutaneous	100%	96.4%	1
- Hematologic	44%	78.6%	0.012
- Renal			
Neutrophils (cells/μl)	16%	17.9%	0.004
- Mild neutropenia (1000-1499)	4%	7.1%	
- Moderate neutropenia (500-999)	4%	39.3%	
- Severe neutropenia (<500)			
Lymphopenia (<1000 cells/μl)	68%	70%	1

Platelets (K/μl)	16%	10.7%	0.859
- Mild thrombocytopenia (50-99)	28%	32.1%	
- Severe thrombocytopenia (<50)			
SLEDAI score	6 (0-23)	6 (1-14)	0.370
SLICC damage index	0 (0-5)	0 (0-6)	0.791
Treatment	24%	53.6%	0.048
- Azathioprine	0%	14.3%	0.113
- Mofetil mycophenolate	4% 56%	35.7% 46.2%	0.006
- Hydroxychloroquine	16%	28.6%	0.553
- Prednisone	28%	25%	
o ≤7.5 mg			
o 7.6-30 mg			
o >30 mg			

Conclusion: The main causes of cytopenias in our SLE patients were disease activity and bone marrow toxicity. Our findings suggest that when patients present with less than 1000 neutrophils/μl, it is unlikely for the cytopenias to be secondary to disease activity. Our study reinforces the diagnostic utility of BMA and biopsy, and the associations we described may assist clinicians to determine the etiology of cytopenias in SLE patients, in order to make appropriate therapeutic decisions.

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THU0261

THE URINARY CELLULAR PROFILE AS A BIOMARKER FOR LUPUS NEPHRITIS

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Background: Proliferative lupus nephritis is one of the most common and serious manifestation of SLE and is a major cause of morbidity. A search for the ideal biomarker for LN is still underway, one that can be used for early detection, and correlate with the class & activity of LN. Urine is normally devoid of leucocytes, however it has been observed that macrophages and T-lymphocytes are routinely present in the urine of LN patients and those with other proliferative renal diseases.⁽¹⁾ This provided the idea for their potential use as biomarkers for proliferative LN.

Objectives: To study the urinary CD4+, CD8+ T Lymphocytes, and CD14 + monocytes in patients with proliferative lupus nephritis, and explore their use as a biomarker for LN.

Methods: Our subjects included 30 patients with biopsy proven proliferative LN and 30 SLE patients without clinical or lab evidence of LN as controls. Lab investigations included serum creatinine, urine analysis, protein creatinine ratio, anti-ds DNA Ab, C3 and C4. For the flowcytometric analysis 100 ml of freshly voided urine in a sterile container were obtained from patients and controls. All samples were processed within 2-4 hours of collection to ensure viability of the cells. Urine mononuclear cell count was done using a hemocytometer. The urine samples were centrifuged then washed twice by phosphate-buffered saline/bovine serum albumin (PBS/BSA) and resuspended in about 300 μl PBS. The cells were stained with anti CD8- FITC, anti CD4- PE, anti CD14-PERCP and anti- CD3-APC monoclonal antibodies. The flow cytometric analysis was done using Becton Dickinson, FACS Calibur multi-parameter flow cytometer equipped with BD CellQuest Pro software for data analysis.

Abstract THU0261 – Figure 1

Results: CD14⁺ cells were the most abundant cells in the urine of LN patients. The mean numbers of urinary CD8⁺, CD4⁺ and CD14⁺ cells/ml were significantly higher in patients with LN (405.6 ± 200.0, 281.1 ± 195.3, and 1554.7 ± 606.8 respectively) than in those without (39.30 ± 17.56, 34.33 ± 16.41, and 161.17 ± 90.91 respectively). AUC for ROC = 1.0 for all 3 markers with CD8⁺ >85 cells/ml, CD4⁺ >80 cells/ml, and CD14⁺ >400 cells/ml being observed exclusively in LN. The cell counts correlated significantly with the protein:creatinine ratio, but not with other markers of disease activity. The CD4:CD8 ratio was significantly lower in LN patients (0.69 ± 0.21) than in those without (0.91 ± 0.31). Urinary CD14⁺ cells seem to occur in much higher counts in Class IV (1736.7 ± 522.0) than Class III LN (898.5 ± 17.68) p=0.084. Figure 1 shows a dot plot of flow cytometric analysis of urinary T cells and monocytes in a patient with lupus nephritis showing increased both CD4⁺ and CD8⁺ T cells and monocytes (dim CD4 expression and CD14 positive (not shown)).

Conclusion: Urinary CD8⁺, CD4⁺ and CD14⁺ cells are highly sensitive and specific markers for detecting proliferative LN. A low CD4:CD8 ratio provides a further clue. The cell counts correlate with proteinuria. CD14 cell counts may be a potential biomarker to differentiate between the different classes of proliferative LN.

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THU0262

FATIGUE IN PRIMARY SJÖGREN'S SYNDROME AS A DISEASE MANIFESTATION REFLECTING THE DEGREE OF MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) INVOLVEMENT

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Background: fatigue in primary Sjögren's syndrome (pSS) is a very common and complex symptom, heavily impairing a wide range of patient functions, quality of life and health policies. To date, measures of fatigue and other patient-reported symptoms/outcomes (PROs) poorly correlate with pSS disease activity assessed by ESSDAI. On the other hand, therapeutic interventions reducing pSS disease activity proved useful to improve fatigue burden in pSS.

Objectives: to evaluate if fatigue correlates to other pSS disease manifestations which may also reflect disease activity, by investigating if: a) higher levels of fatigue shows a higher frequency of a heavier involvement of mucosa-associated lymphoid tissue (MALT) documented by histopathology, persistent glandular swelling, or cryoglobulinemia (1); and b) if fatigue correlates to other pSS-related somatic symptoms, such as dryness and arthralgias.

Methods: among pSS patients undergoing clinical evaluation in our Sjögren's Clinic in a six-months period, 86 consecutive unselected patients, fulfilling the latest ACR/EULAR pSS classification criteria, accepted to report their degree of fatigue, general dryness, ocular dryness, oral dryness and pain on 10-cm VAS (range 0-100), and to complete the ESSPRI (range 0-10), the PROFAD-SSI-SF (range 0-28) and the EQ-5D-scale (0-100) questionnaires. Four subgroups of fatigue severity were preliminary defined (2), presenting, as previously described (3): no fatigue (VAS=0): 12.8% (n=11); low fatigue (VAS=1-24): 25.3% (n=19); moderate fatigue (VAS=25-74): 58.7% (n=44); high fatigue (VAS=75-100): 16% (n=12). As previously reported (3) no significant age or sex difference was present between subgroups, and potential contributors to fatigue, such as autoimmune thyroiditis, anemia and fibromyalgia did not play a role.

The frequencies of peculiar manifestations related to an increased activity in MALT involvement in pSS, such as persistent salivary gland swelling, cryoglobulinemia and biopsy-proven diagnosis of myoepithelial sialadenitis (MESA) or of pSS-related MALT lymphoma, at any time in the clinical history of patients, were evaluated for each subgroup.

Secondly, the correlations between fatigue VAS and PROs reflecting somatic symptoms were performed.

Results: pSS patients reporting moderate or high fatigue VAS showed significantly higher frequencies of salivary gland swelling (p=0.0274), of MESA or lymphoma proven by histological diagnosis (p=0.0397), if

compared to pSS patients with no or low levels of fatigue. Cryoglobulinemia was not significantly increased, although more frequent, in patients with moderate or high fatigue (10.7%) compared to patients with no or low fatigue (6.6%).

Fatigue VAS score did not correlate with ESSDAI.

Patients with higher levels of fatigue showed significant (p<0.0001) higher scores in total ESSPRI, dryness-ESSPRI, pain-ESSPRI, ocular dryness VAS, oral dryness VAS, pain VAS, somatic fatigue domain of PROFAD, arthralgia domain of PROFAD, total SSI and PROFAD-SSI-SF.

Finally, patients with higher levels of fatigue reported worst scores in quality of life EQ-5D-scale.

Conclusion: The severity of fatigue appears to mirror the degree of MALT involvement, and this involvement is the biological substrate of pSS itself. This represents a demonstration that fatigue is biologically related to pSS, and supports the notion that fatigue should be treated by disease-modifying drugs rather than only with symptomatic therapies in pSS. In addition, dedicated scores of pSS activity can be developed for pSS patients where fatigue is one of the dominant symptoms. Since fatigue may also correlate with pSS somatic symptoms, such as dryness and arthralgia, they could also be included.

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THU0263

NOVEL SUBSETS OF SLE PATIENTS ENRICHED FOR RENAL MANIFESTATIONS IDENTIFIED BY CLUSTERING WITH EXPANDED AUTOANTIBODY PROFILES OF NATIVE AMERICAN (NA), AFRICAN AMERICAN (AA), AND EUROPEAN AMERICAN (EA) SLE PATIENTS

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Background: Autoantibodies (AABs) are a hallmark of systemic lupus erythematosus (SLE). Common SLE AABs show differences in specificities, levels and associations with clinical characteristics of disease which may be influenced by ethnicity.(1-2) NA SLE patients do not always exhibit classical AAB profiles.(2) Understanding how AAB profiles associate with clinical disease, including in NA patients, is important to better inform disease management.

Objectives: To identify patient subsets enriched for renal disease by clustering NA, AA and EA SLE patients into more homogeneous disease subsets based on expanded AAB profiles.

Methods: Serum samples from 49 NA, 49 AA, and 49 EA age, sex and ANA titer-matched SLE patients who met ACR classification and 10 sex and age matched controls from each ethnicity were tested for AAB reactivity by autoantigen microarray. Normalized fluorescence intensity (NFI) for AAB binding was determined for each individual for all autoantigens. Ratios of NFIs to total IgG were calculated and converted to Z-scores. Kruskal-Wallis analysis of Z-score transformed AAB ratios were used to identify AABs that differed significantly between patients and controls for each ethnicity; these AABs were used for hierarchical clustering of SLE subjects within each ethnicity. The enrichment of SLE clinical criteria within each cluster was determined by Fisher's exact test.

Results: AABs to nucleic acids and Ro52 were present in SLE patients of all three ethnicities. On average, NA SLE patients, but not EA or AA SLE patients, had lower levels of AABs against extracellular matrix (ECM) antigens compared to controls. AA and EA, but not NA, SLE patients had significantly higher levels of AABs to Sm, RNP and histones compared to matched controls. In each ethnicity four clusters of SLE subjects were identified by ethnicity-specific AABs. All three groups had a cluster of subjects enriched in nucleic acid-specific AABs and a cluster of subjects enriched in Ro52 AABs. The NA group also had two clusters enriched in ECM AABs. The AA group had an Sm/RNP AAB enriched cluster and a nucleolin/histone AAB enriched cluster. Two additional EA