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FRI0292 ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN (APS/PT) ANTIBODIES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: Several studies have showed conflicting results regarding the presence and meaning of anti-phosphatidylserine/prothrombin (aPS/PT). However aPS/PT antibodies seem to be a risk factor for thrombosis. Nevertheless, most of the studies have focused on patients with SLE and secondary antiphospholipid syndrome (APS).
Objectives: To assess the prevalence of aPS/PT antibodies, as well as their association with other antiphospholipid (aPL) antibodies (specially lupus anticoagulant [LA]) and thrombosis, in a well-established cohort of primary APS from a single center.
Methods: We included 96 consecutive patients with primary APS according the Sydney classification criteria and/or patients with hematological features (thrombocytopenia and hemolytic anemia) attending a referral center in Mexico City. Patients from both groups fulfilled the Sydney laboratory criteria for APS. We registered demographics, disease duration and type of manifestation. aCL (IgG and IgM), antibodies to purified human anti-β2GP-I (IgG and IgM) and aPS/PT antibodies (IgG and IgM) were assessed by ELISA (INOVA Diagnostics). LA was determined by LA/1 screening reactant and a confirmatory test LA/2 according to published guidelines. We used chi-square ($\chi 2$) test, Spearman correlation analysis and logistic regression.
Results: Most patients were females (69.7%), mean age 44.5±14.6 and median disease duration 7.3 years. The main clinical features were thrombosis (n=74, 77%), hematologic involvement (n=49 patients, 51%) and obstetric events (n=24, 25%) (non-exclusive groups). The prevalence of LA was 69.8%, aCL-IgG 56.8%, anti-β2GP-I IgG 43.1%, aCL-IgM 31.5% and anti-β2GP-I IgM 21%. The frequency of aPS/PT antibodies was 61.2% and 61.6% for IgG and IgM isotype, respectively. When we compared patients with LA+ (n=58) vs. LA- (n=25), the first group had a higher prevalence of aPS/PT-IgG (79.3% vs.16%, p=0.0001) and aPS/PT-IgM antibody (81.5% vs. 31.8%, p=0.001), as well as higher titers (aPS/PT-IgG 130.5 U vs. 8.2 U and aPS/PT-IgM 58.5 U vs. 16.6 U, p=0.0001). aPS/PT-IgG antibodies correlated with aPS/PT-IgM (ρ=0.59, p=0.0001), aCL-IgG (ρ=0.62, p=0.0001), anti-β2GP-I IgG (ρ=0.63, p=0.001) and anti-β2GP-I IgM (ρ=0.35, p=0.001). On the other hand, aPS/PT IgM antibodies correlated with aCL-IgG (ρ=0.57, p=0.0001), aCL-IgM (ρ=0.42, p=0.001), anti-β2GP-I IgG (ρ=0.48, p=0.001) and anti-β2GP-I IgM (ρ =0.59, p=0.0001). We found moderate agreement between the presence of LA and both aPS/PT isotypes (k=0.58 p=0.0001 for IgG, and k=0.47 p=0.001 for IgM). Thrombosis was associated with aPS/PT-IgG antibodies (87.7% vs. 61.1%, p=0.003) but not with aPS/PT IgM (73.6% vs. 81.8%, p=0.37). At the logistic regression analysis, the aPS/PT IgG antibodies remained associated with thrombosis after adjusting by all other aPL antibodies, OR 8.6 95% CI 2.1–33.8, p=0.002.
Conclusions: In this cohort of patients with primary APS, aPS/PT antibodies were highly prevalent, correlated with other aPL antibodies and were associated independently with thrombosis.
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FRI0293 CHARACTERIZATION AND RISK ESTIMATE OF CANCER IN PRIMARY SJÖGREN SYNDROME: ANALYSIS IN 1300 PATIENTS

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Objectives: To characterize the risk of solid and hematological cancer in a large, well-characterized cohort of patients with primary Sjögren syndrome (SjS).
Methods: The GEAS-SS multicenter registry is a network of Spanish reference centers with specific clinical experience in the management of SjS patients. By January 2016, we had analyzed the development of cancer in 1300 consecutive patients fulfilling the 2002 SjS classification criteria. Multivariate Cox proportional-hazards regression analysis allowed adjustment for age at diagnosis, gender and the statistically-significant baseline variables associated with cancer in the univariate analysis. The sex- and age-specific incidence rates (SIR) of cancer were estimated from 2012 Spanish mortality data modeling, using a set of age-, sex- and site-specific incidence:mortality ratios.
Results: After a mean follow-up of 91 months (9922.3 person-years), 127 (9.8%) patients developed 133 cancers. The most frequent type of cancer was B-cell lymphoma (34% of cancers, including 27 MALT and 19 non-MALT B-cell lymphomas). Systemic activity at diagnosis of primary SjS correlated with the risk of hematological neoplasia (HR 1.06, $p<0.001$). Positive cryoglobulins at SjS diagnosis were associated with a high risk of either B-cell or non-B-cell lymphoma subtypes. Patients with cytopenias had a high risk of non-MALT B-cell and non-B-cell cancer, while those with low C3 levels had a high risk of MALT lymphomas and those with monoclonal gammopathy and low C4 levels had a high risk of non-MALT B-cell lymphomas. The estimated SIR for solid cancer was 1.13 (95% CI 0.88–1.46) and 11.02 (95% CI 8.35–14.54) for hematological cancer. SIRs for specific cancers were 36.17 (95% CI 25.44–51.43) for multiple myeloma and immunoproliferative diseases, 19.41 (95% CI 7.29–51.72) for Hodgkin lymphoma, 6.04 (95% CI 3.43–10.64) for other non-Hodgkin lymphomas, 5.17 (95% CI 1.94–13.79) for thyroid cancer, 4.81 (95% CI 1.81–12.83) for cancers of the lip and oral cavity and 2.53 (95% CI 1.05–6.07) for stomach cancer.
Conclusions: One third of cancers developed by patients with primary SjS are B-cell lymphomas. The prognostic factors identified at SjS diagnosis differed according to the subtype of B-cell lymphoma developed. Primary SjS is also associated with an enhanced risk of development of some types of non-hematological cancers (thyroid, oral cavity and stomach).
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FRI0294 ULTRASOUND OF THE SALIVARY GLANDS HELPS TO DISTINGUISH BETWEEN PRIMARY AND SECONDARY SJÖGREN SYNDROME

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Background: Previous studies have demonstrated typical findings in the ultrasound of salivary glands (USG) in patients with primary Sjögren syndrome (pSS) compared with healthy controls. However, it is unknown, if these findings are only seen in patients with pSS but also in patients with secondary Sjögren syndrome (sSS) or other connective tissue diseases with positive Ro-SSA/La-SSB antibodies.
Methods: We used an ultrasound score developed by Zhang [1] to investigate salivary glands with a score ranging from 0–48. We compared the score from patients with pSS according the criteria of the American-European Consensus Group (group 1) with patients who fulfilled the clinical criteria (1–4), but were Ro-SSA/La-SSB negative (group 2), with patients who had another rheumatic disease, but had sicca symptoms and were Ro-SSA and/or La-SSB positive (sSS) (group 3), with patients with other rheumatic disease without Ro-SSA or La-SSB antibodies (group 4), with patients with other rheumatic disease with Ro-SSA antibodies but no sicca symptoms (group 5) and with patients with no rheumatic disease (group 6), respectively. We investigated the parotid and the submandibular salivary glands bilaterally. The USG was assessed with a score from 0–48 points with a maximum of 12 points for 4 items each (hyoechoic areas, hyperechoic reflexes, inhomogeneity and distinct organ border). If available the score was correlated with the scintigraphically measured function of the salivary glands.
Results: We included USG of 92 patients in our study. Group 1 (n=33) had a score of 16.6±11.6; group 2 (n=7) 2.4±3.5; group 3 (n=16) 8.6±9.5; group 4 (n=16) 5.3±7.8; group 5 (n=11) 4.5±6.7 and group 6 (n=9) 1.5±2.3, respectively. The score between group 1 and all other groups was significantly different ($p<0.01$), with no significant differences between all other groups. In 25 patients a scintigraphy of the salivary glands was available. The excretory function in the scintigraphy highly significantly correlated with the ultrasound score (r=0.53, $p<0.001$).
Conclusions: USG showed significantly higher scores in patients with pSS, than in patients with sSS or other rheumatic disease. USG as a non invasive investigation might be similarly helpful for the diagnosis of pSS like salivary gland functional tests. USG findings can reliable distinguish between pSS and sSS associated with other rheumatic disease, also if they are positive for Ro-SSA/La-SSB.

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FRI0295 HIGH RISK OF IDIOPATHIC OSTEONECROSIS IN SLE PATIENTS WITH HIGH ANTIPHOSPHOLIPID SCORE AND HYPERTRIGLYCERIDEMIA

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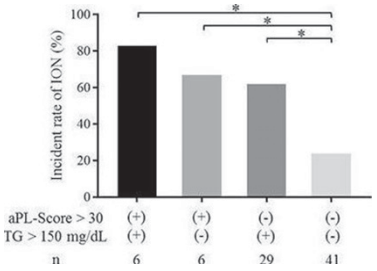
Background: Systemic lupus erythematosus (SLE) patients are prone to develop idiopathic osteonecrosis (ION) compared to other connective tissue disease patients or healthy subjects. ION has been shown to occur as a result of ischemia, however, the involvement of antiphospholipid antibodies (aPL) in its pathophysiology remains to be elucidated. In the last years, our group introduced a quantitative marker of aPL "antiphospholipid score (aPL-S)", which well reflected the risk of developing thrombosis [1].
Objectives: We aimed to identify the impact of aPL on the development of ION using aPL-S.
Methods: A single center retrospective study comprising 82 consecutive patients who were diagnosed SLE at the Rheumatology department of Hokkaido University Hospital and underwent magnetic resonance imaging (MRI) of hip joints from January 2000 to December 2016. Among all the enrolled patients, aPL-S, which is calculated from 0 to 86, as well as classical risk factors for ION were evaluated.
Results: All 82 patients (13 males and 69 females) were given glucocorticoids. ION of the femoral head was diagnosed by MRI scan in 37 patients. Male (ION(+): ION(-) 10/37 (27%) vs 3/45 (7%), p=0.016), malar rush (ION(+): ION(-) 22/37 (59%) vs 16/45 (36%), p=0.045), aPL positivity (ION(+): ION(-) 22/37 (59%) vs 15/45 (33%), p=0.026), high aPL-S (>30) (ION(+): ION(-) 9/37 (24%) vs 3/45 (7%), p=0.031), hypertriglyceridemia (fasting triglyceride levels >150 mg/dL) (ION(+): ION(-) 23/37 (62%) vs 12/45 (27%), p=0.002) and high dose of glucocorticoids (equivalent to 0.8mg/kg or more prednisolone) (ION(+): ION(-) 34/37 (92%) vs 21/45 (47%), p<0.001) were identified as risk factors for ION at univariate analysis. Multivariate analysis confirmed high aPL-S (OR 5.27; 95% CI 1.08 to 34.52, p=0.040), hypertriglyceridemia (OR 5.66; 95% CI 1.79 to 20.73, p=0.003) and high dose of glucocorticoids (OR 16.11; 95% CI 4.01 to 92.54, p<0.001) as independent variables. Of note, in 6 patients who had both high aPL-S and hypertriglyceridemia, 83% (5/6) developed ION (Figure 1). Conversely, systemic lupus erythematosus disease activity index and pulsed methylprednisolone therapy were not identified as risk factors for ION.



Conclusions: We newly identified high aPL-S as a risk factor for ION. Furthermore, SLE patients who have both high aPL-S and hypertriglyceridemia are at very high risk of ION. These findings suggest the involvement of microvascular occlusion in the pathophysiology of ION in SLE.
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FRI0296 SINGLE CENTER EXPERIENCE WITH 300 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with diverse clinical manifestations.
Objectives: Here, we present 300 patients with SLE attending our clinic between 2001 and 2017.
Methods: Demographics, clinics, laboratory findings, Systemic Lupus International Clinics (SLICC)/American College of Rheumatology (ACR) damage index scores and treatments were analyzed. Diagnosis was confirmed with 1997 ACR (1) or 2012 SLICC (2) classifications. Descriptive statistical tests were used for analysis.
Results: Demographics and clinical characteristics are presented in Table 1. Anti-dsDNA was positive in 185 (61.6%), anti-Sm was positive in 35 (11.6%), anti-phospholipid antibodies was positive in 67 (22.3%), direct Coombs test was positive in 69 (23%) patients. Complement levels were low in 171 (57%) patients. In patients with renal disease, class IV lupus nephritis was the most common form (37 patients [12%]) followed by class II nephritis (34 patients [11%]). Forty-six patients had antiphospholipid syndrome. Treatments patients ever received are presented in Table 2. Cyclophosphamide treatment was given mostly for renal disease. Within 22 patients receiving rituximab, 2 had thrombocytopenia and 1 had hemolytic anemia unresponsive to other treatments, 1 had protein-losing enteropathy and 1 had lupus enteritis; the rest had lupus nephritis. One patient received intravenous immune globulin (IVIG) for severe neutropenia and 2 patients for severe thrombocytopenia. One patient received plasmapheresis for vasculitis. One patient received IVIG, plasmapheresis, rituximab for severe renal failure, alveolar hemorrhage requiring intensive care unit admission and 1 patient received same treatment for severe unresponsive hemolytic anemia.

Table 1. Demographics, clinical characteristics of patients

Age (years)	46±13 (min-max: 20–83; median: 45)
Duration of follow up (months)	58±52 (min-max: 1–180; median: 48)
Gender (Female/Male)	267 (89%)/33 (11%)
Muco-cutanous (n, %)	214 (71.3%)
Arthritis (n, %)	198 (66%)
Renal disease (n, %)	121 (40.3%)
Leukopenia/lymphopenia (n, %)	200 (66.6%)
Hemolytic anemia (n, %)	19 (6.3%)
Thrombocytopenia (n, %)	58 (19.3%)
Serositis (n, %)	55 (18.3%)
Nervous system disease (n, %)	24 (8%)
Anti-phospholipid Syndrome (n, %)	46 (15.3%)

Table 2. Treatment

Steroid/pulse treatment (n, %)	294 (98%)/65 (21.6%)
Hydroxycholoroquine (n, %)	300 (100%)
Azathioprine (n, %)	196 (65.3%)
Mycophenolate mofetil (n, %)	83 (27.6%)
Cyclophosphamide (iv) (n, %)	78 (26%); 10±4.5 cycles (min-max: 2–17)
Rituximab (n, %)	22 (7.3%)
Intravenous immunglobulin (IVIG) (n, %)	7 (2.3%)
Plasmapheresis (n, %)	4 (1.3%)

Conclusions: In long term, SLICC/ACR damage index was highest in patients received pulse steroid for renal disease (min:0, max:5). Four (1.3%) patients had pulmonary hypertension, 31 (10.3%) had avascular necrosis, 24 (8%) had viral infections requiring treatment or bacterial infections requiring admission due to immunosuppression, 12 (4%) had malignancy. SLE is an autoimmune disease requiring multi-faceted approach.
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FRI0297 ROLE OF SERUM INTERLEUKIN-6 IN BLOOD BRAIN BARRIER DAMAGES IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuropsychiatric manifestation in systemic lupus erythematosus (NPSLE) is one of the most serious complications of the disease. We have recently demonstrated that the breakdown of blood brain barrier (BBB) plays a crucial role in the development of diffuse psychiatric/neuropsychological manifestations (diffuse NPSLE), allowing influx of neuron-reactive autoantibodies from systemic circulation into the brain. However, the mechanism of BBB damages remains unclear. On the other hand, although CSF interleukin-6 (IL-6) has been shown to be elevated in NPSLE, there has been no report on serum IL-6 in NPSLE.
Objectives: The present study was designed in order to elucidate the roles of serum IL-6 in the pathogenesis, especially in development of BBB damages, In NPSLE.
Methods: Paired serum and cerebrospinal fluid (CSF) samples were obtained from 101 SLE patients when they presented active neuropsychiatric manifestations (69 patients with diffuse psychiatric/neuropsychological syndromes [diffuse NPSLE] and 32 patients with neurologic syndromes or peripheral nervous system involvement [focal NPSLE]) and from 22 non-SLE control patients with non-