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

FRI0144

SEROLOGICAL EVOLUTION IN PATIENTS WITH POSITIVE ANTIPHOSPHOLIPID ANTIBODIES- A RETROSPECTIVE STUDY OF CHINESE COHORT

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Background: Antiphospholipid antibodies (aPLs) and thrombotic/obstetric events are the characteristics the antiphospholipid syndrome. The titers of aPL sometimes may decrease and become negative during the follow-up period. Whether the negativization being related with a lower risk of thrombotic events, allowing for withdrawal of anti-coagulant therapy is controversial. And the factors associated with each aPL negativization are still unknown.

Objectives: To explore the clinical and serological course of patients with positive aPLs, and the factors and therapeutic implications associated with aPL negativization.

Methods: Patients with a persistent positive aPL serology according to established criteria between 1997 and 2018 were included. The test of Lupus anticoagulant (LA), anti-cardiolipin antibody (aCL) and anti-β2 glycoprotein I (anti-β2GP1) were following the International Society on Thrombosis and Haemostasis guidelines. The patients were classified as aPL negativization if the following aPL tests became negative, on two or more occasions at least 12 weeks apart. Titer more than 40RU/ml was defined as moderate to high titer for aCL and anti-β2GP1. For patients receiving warfarin, the results of LA were counted only when INR<1.5.

Results: The baseline characteristics of 93 patients were shown in Table 1. After a mean follow-up of 45.0 (45.0) months, the percentage of aPL negativization was 10.8% (9/83), 26.1% (18/69), 24.5% (13/53) for LA, aCL and anti-β2GP1 respectively (Figure 1). Patients with triple aPL positivity at baseline were associated with persistently positive serology for all the three aPLs. Multivariate analysis confirmed that double positive of two methods (dVRR and SCT) was the only independent protective factor for LA negativization (OR 0.055; 95%CI: 0.006-0.545; p=0.013). SLE, moderate to high titer of aCL and number of baseline aPL positivity were independently associated with aCL negativization (OR 18.2; 95%CI: 1.45-228; p=0.025, for SLE; OR 0.217; 95%CI: 0.053-0.888; p=0.034, for moderate to high titer of aCL; OR 0.198; 95%CI: 0.057-0.689; p=0.011, for number of baseline aPL positivity). Moderate to high titer of anti-β2GP1 and number of baseline aPL positivity were independently protective factors for anti-β2GP1 negativization (OR 0.168; 95%CI: 0.032-0.872; p=0.034, for moderate to high titer of anti-β2GP1; OR 0.243; 95%CI: 0.073-0.813; p=0.022, for number of baseline aPL positivity). Unfortunately, we didn't find any relationship between aPL persistent positivity and further thrombosis/pregnancy morbidity due to limited events.

Table 1. The baseline characteristics of aPL positive patients

baseline characteristics	n=93
Female, n(%)	82.0 (88.2)
Age, mean±SD	33.7±13.8
Disease duration, median(IQR)	68.0 (85.0)
Follow-up period, median(IQR)	45.0 (45.0)
Thrombotic events, n(%)	29.0 (31.2)
Obstetric events, n(%) (n=82)	25.0 (26.9)
Non-criteria manifestations, n(%)	45.0 (48.4)
SLE, n(%)	62.0 (66.7)
Number of aPL positivity, median(IQR)	2.00 (1.00)
aPL triple positivity, n(%)	40.0 (43.0)

Conclusion: The proportion of aCL and anti-β2GP1 negativization are higher than LA. The number of positive antibodies and higher antibody load are associated with persistently positive serology. Patients with SLE were easier to get aCL negativization.

Figure 1 The positivity of aPLs at baseline and the serological evolution during the follow-up.

Disclosure of Interests: None declared

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FOLLOW-UP OF A MONOCENTRIC COHORT OF SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME

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Background: Seronegative antiphospholipid syndrome (SN-APS) is the term proposed to describe patients with clinical signs highly suggestive of APS but persistently negative for conventional antiphospholipid antibodies (aPL) assays. Therefore, new antigenic targets or different methodological approaches have been investigated to detect aPL in SN-APS [1].

Objectives: The aim of this study was to describe the clinical follow-up of a monocentric cohort of SN-APS patients.

Methods: The study included all consecutive SN-APS patients examined from 2014 to 2018. In all patients other possible causes of thrombosis or obstetric morbidity were ruled out. APL were investigated through two tests: 1. anti-cardiolipin/vimentin antibodies (aCL/Vim) by enzyme-linked immunosorbent assay (ELISA) 2. anti-cardiolipin antibodies (aCL) by thin-layer chromatography (TLC)-immunostaining.

Results: We enrolled 121 patients (all Caucasian except one Asian and one Hispanic women). Clinical and demographic characteristics are reported in Table 1.

Table 1. Clinical and demographic characteristics

Features	SN-APS n= 121 (%)
Male/Female	14/107
Mean age in years (from-to)	42.58 (16-78)
PAPS/SAPS	78/43 (64.5/35.5)
SLE	28 (23.1)
Others autoimmune diseases	15 (12.4)
Pregnancy morbidity	56/107 (52.3)
Spontaneous abortions	49 (45.8)
Normal fetus deaths	22 (20.6)
Premature births	7 (6.54)
Thrombosis	72 (59.5)
Arterial thrombosis	36 (29.8)
Venous thrombosis	48 (39.7)
Recurrent thrombosis	28 (23.1)
Thrombosis + Pregnancy morbidity	8 (6.6)
Non-criteria APS features	45 (37.2)
Livedo reticularis	18 (14.9)
Thrombocytopenia	12 (9.9)
Migraine	19 (15.7)
Seizures	5 (4)
Others	11 (9)
Cardiovascular risk factors	50 (41.3)
Hypercholesterolemia	8 (6.6)
Smoking	22 (18.2)
Hypertension	22 (18.2)
OC/HRT	7 (5.8)
Diabetes	4 (3.3)

Sixty-nine out 121 patients (57%) resulted positive for at least one non-conventional test in two occasions more than 12 weeks apart (Figure 1). The agreement between first and second test resulted respectively of K=0.703 e K=0.655 (Cohen's K test). Figure 2 shows the prevalence of aCL (TLC-immunostaining) and aCL/Vim. We found a significant correlation between aCL (by TLC-immunostaining) and aCL/Vim ($p = 0.027$), brain MRI ischemic changes ($p = 0.012$) and age ($p = 0.023$). aCL/Vim was significantly correlated with livedo reticularis ($p = 0.015$). Patients with double positivity showed a higher prevalence of mixed thrombotic and obstetrical features than patients with single positivity ($p < 0.001$, likelihood positive ratio 8.2).

Non-conventional aPL positivity better supported the diagnosis of APS and, following the therapeutic changes implemented, in a median follow up of 41 months (IQR 39.5) only 3 cases of recurrent thrombosis (2 cases of arterial thrombosis during treatment with antiaggregant therapy and one case of venous thrombosis in treatment with new oral anticoagulant therapy) were observed. During the follow-up, 35 patients with obstetric morbidity who resulted positive for the tests had 20 pregnancies; 12 of them (60%) experienced a good outcome under conventional treatment for classical APS.

Conclusion: The results demonstrate that new methods – TLC-immunostaining – or new antigens - CL/Vim – allow to detect aPL in so-called “SN-APS” patients and, consequently, to prescribe the most appropriate therapy.

References:

[1] Conti F et al. The Mosaic of “Seronegative” Antiphospholipid Syndrome. J Immunol Res. 2014;2014:389601

Fig.1 The prevalence of autoantibodies in SN-APS **Fig.2** The percentage of SN-APS positive for more than one test

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SLICC/ACR DAMAGE INDEX IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME WITH AND WITHOUT SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The role of antiphospholipid syndrome (APS) as a cause of chronic organ damage in patients with systemic lupus erythematosus (SLE) is important. While acute disease manifestations of APS are well known, information on the long-term prognosis and damage in affected patients is still very limited.

Objectives: To assess the severity of organ damage in patients with APS without SLE and with concomitant SLE, as well as the feature of irreversible damage to internal organs in patients with primary APS during a dynamic observation using SLICC/ACR Damage Index (SDI).

Methods: The study included 195 patients (41 men and 154 women) who were observed at the Institute of Rheumatology from 2007 to June 2018 with a diagnosis of SLE and APS. The study inclusion criteria were: a follow-up period of at least 3 years with the study of serological markers of APS for previous years, the possibility of dynamic monitoring of patients, patient consent. Patients were divided into 3 groups, depending on presence of APS: group I - SLE with APS (n=99 with average age 34.6 [25-44]), group II - SLE without APS (n=45; 33.5[26-42]) and group III - 45 (average age 37.7 [27-46]) patients with primary APS (PAPS) diagnosed according to international diagnostic criteria, without signs of any disease. In all three groups organ damage was assessed using SDI. SDI 1-2 points corresponded to moderate damage, more than 2 points - to severe.

Results: A linear increase in irreversible organ damage was noted over 10 years of follow-up. At the time of inclusion in the study, the average SDI was significantly higher in the SLE + APS group than in the SLE group: 1.32 versus 0 when included ($p < 0.0001$). A direct correlation was found between the age of patients and the value of SDI both in the group I ($p = 0.004$, $r = 0.284$) and in the group II ($p = 0.04$, $r = 0.281$) when included in the study. There was a direct correlation between the activity of the disease on the SLEDAI at the end of the study and the value of SDI ($p = 0.03$, $r = 0.41$) in the group II. The number of patients by the 10th year of follow-up remained in group I were 44 of 99, in group II - 24 of 51 and in group III - 14 of 45. SDI was more than 2 points in 39 (89%) of 44 patients in group I, in 12 (50%) of 24 in group II and 9 (65%) of 14 in Group III ($p = 0.0002$ OR=13; 95% CI 2.4-70). 5 years after the start of the observation average SDI in group I and II was 2.5 and 1.3 ($p < 0.0001$) and after 10 years - 2.8 and 1.9 ($p = 0.0008$) accordingly. An increase of total SDI occurred primarily due to damage to peripheral vessels due to the large number of thromboses (in 55% of patients) in the group II. Using step-by-step multiple logistic regressions in the study groups only APS was an independent predictor of increased SDI. The most common cause of an increase in SDI in the PAPS group was damage to peripheral vessels (64%) as a result of a high frequency of venous thrombosis, followed by damage to the neuropsychiatric system (55%) and the cardiovascular system (40%).

Conclusion: APS is an independent predictor of increased SDI. The determination of irreversible organ damage in patients with PAPS using SDI allows us to assess the functional disorders of organs and systems and can be used in clinical practice in these patients.

Disclosure of Interests: None declared

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FRI0147

PREVALENCE OF COMORBIDITIES IN ANTIPHOSPHOLIPID SYNDROME VERSUS RHEUMATOID ARTHRITIS: A MULTICENTRE, AGE- AND SEX-MATCHED STUDY

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Background: Comorbidities in rheumatic diseases (RDs) have been associated with increased morbidity and mortality. Evidence on prevalence of comorbidities in antiphospholipid syndrome (APS) and its difference from high comorbidity burden RDs is limited.

Objectives: To compare the prevalence of common comorbidities between APS [primary (PAPS) and Systemic lupus erythematosus (SLE)-APS] and Rheumatoid arthritis (RA) patients.

Methods: 326 APS patients from the Greek registry (237 women, mean age 48.7±13.4 years, 161 PAPS) were matched 1:2 for age and sex with 652 RA patients from Greek RA Registry. Prevalence of cardiovascular (CV) risk factors, stroke, coronary artery disease (CAD), osteoporosis, diabetes mellitus (DM), Chronic obstructive pulmonary disease (COPD), depression and neoplasms were compared between APS and RA using logistic regression analysis.

Results: Regarding CV burden, hyperlipidemia and obesity (BMI≥30) were comparable while hypertension, smoking, CAD and stroke were more prevalent in APS compared to RA patients (Table 1). Osteoporosis and depression were more frequent in APS while DM, COPD and neoplasms were comparable between two groups. Comparison of APS subgroups to 1:2 matched RA patients revealed that smoking and stroke were more prevalent in PAPS and SLE-APS vs RA. Hypertension, CAD and osteoporosis were more prevalent only in SLE-APS vs. RA while DM was less prevalent in PAPS vs. RA patients.