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

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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