history of vascular thrombosis (VT) from those with pregnancy morbidity (PM). Of the five domains of β2GPI, pathogenic IgG aPL are considered to target Domain I (DI). We have developed a direct anti-DI ELISA using bacterially expressed DI. Here we investigate whether IgG, IgM and IgA anti-DI levels correlate with IgG, IgM and IgA anti-β2GPI and which of these tests correlate best with clinical phenotypes.

Methods: We used 9 different ELISAs (IgG/IgM/IgA for each of aCL, aβ2GPI and aDI) to test 168 serum samples - 53 from patients with APS (F:M 46:7, mean age 45.6 ± 12.0); 80 with SLE but not APS (F:M 75:5, mean age 35.0 ± 11.4); and 35 healthy controls (HC) (F:M 23:12, mean age 31.0 ± 7.2). Of 53 APS subjects, 27 suffered VT only, 13 PM only, and 13 both. IgG/IgM/IgA aCL activity was defined as G/M/A-PLU respectively. For all remaining assays, results were expressed in units of activity by reference to an in-house standard. Univariate analysis was performed using one-way ANOVA to determine which assay(s) best differentiate APS from SLE and HC, and whether any were associated with the VT or PM phenotypes within APS.

Results: All 9 assays gave significantly higher antibody titres in APS compared to SLE and HC ($p < 0.0001$ in all cases). For 4 of these 9 assays, titres were raised in SLE compared to HC, thus only 5 assays (IgM aCL, IgG/IgM/IgA aβ2GPI and IgG aDI) selectively recognized APS-derived sera. In the APS group, there was a strong correlation between aβ2GPI and aDI for IgG ($p = 0.0002$, $r = 0.6390$) and IgA ($p = 0.0001$, $r = 0.7771$) but not IgM. In contrast, there were no correlations between aβ2GPI and aDI in the SLE group. Although none of the aβ2GPI assays nor IgG aDI could discriminate between patients with VT compared to PM, IgA aDI was found to be associated with VT ($p \leq 0.01$).

Conclusions: To our knowledge, this is the first study to measure IgG/IgM/IgA aPL against CL, β2GPI and DI simultaneously. aβ2GPI of all isotypes and IgG aDI were found to be most specific for APS. The correlation between aβ2GPI and aDI in APS, but not non-APS subjects supports the idea that pathogenic aβ2GPI bind specifically to DI. The finding that IgA aDI shows a specific association with VT is interesting but needs to be repeated in larger studies.

Disclosure statement: All authors have declared no conflicts of interest.

342. INTERFERON-MEDIATED VASCULAR DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS: FAILURE OF ENDOTHELIAL REPAIR RATHER THAN DIRECT ENDOTHELIAL TOXICITY?

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Background: Patients with Systemic Lupus Erythematosus (SLE) demonstrate increased endothelial dysfunction and a significantly increased risk of premature cardiovascular disease (CVD) compared to healthy control subjects. Type-1 interferons (IFN) are the dominant inflammatory cytokines in SLE. IFNα therapy can induce endothelial dysfunction in patients with viral hepatitis, although the mechanism by which this occurs is unknown. It has been proposed that IFNα contributes to vascular damage by inhibition of endothelial repair mechanisms. IFN has been shown to impair the function of endothelial progenitor cells (EPCs) in vitro, replicating a lupus EPC phenotype. We aimed to determine whether a directly toxic effect of IFN upon mature endothelial cells may also contribute to endothelial dysfunction in SLE.

Methods: Human aortic endothelial cells (HAoECs) were cultured in standard conditions. Circulating Angiogenic Cells (CACs) were obtained by culture of peripheral blood mononuclear cells on human fibronectin in endothelial culture media. The effect of IFNFα2b on HAoECs was measured in terms of: proliferation (cell counting and MTT assay), nitric oxide bioavailability (Griess assay of culture supernatant) and capillary-like network formation (2D in Matrigel and 3D in type-1 rat tail collagen gel). An Affymetrix GeneChip Human Exon 1.0 ST Array was used to determine changes in gene expression at 6 hours following addition of IFNα2b. The effect of IFNFα2b on CAC cell number and morphology was studied.

Results: IFNα2b at concentrations of 0.1-100 ng/ml had no effect on HAoEC proliferation measured by either cell count or MTT assay at up to 72 hours ($n = 3$ for each). The expression of 164 genes was significantly changed (>2-fold change, $q < 0.2$) by the addition of 10 ng/ml IFNα2b at 6 hours. These genes were primarily those previously reported to be regulated by IFNα (e.g. IFIT1, IFI44L, MX1) or those involved in cellular response to virus.

Nitric oxide availability unchanged by the addition of IFNα2b ($n = 3$). The formation of 2-dimensional capillary networks in Matrigel was variable and not consistently impaired by the addition of 10 ng/ml IFN. Furthermore the development of 3-dimensional networks in collagen was not disrupted by the addition of IFNα2b to either the gel or the culture media.

CAC cell number was dramatically reduced by IFNα2b and was specifically associated with loss of spindle-shaped cells.

Conclusions: Interferon α2b did not affect the function of HAoECs in vitro. Gene expression was not influenced beyond those genes important in response to virus. We propose therefore that IFN-mediated vascular damage is secondary to impaired endothelial repair rather than direct IFN toxicity. This has implications for the development of in vitro endothelial models relevant to SLE and the prevention of CVD in lupus.

Disclosure statement: All authors have declared no conflicts of interest.

343. SOLUBLE VASCULAR CELL ADHESION MOLECULE-1 LEVEL IN PATIENTS WITH ANTHIPHOSPOLIPID SYNDROME: ITS ASSOCIATION WITH DISEASE ACTIVITY AND ENDOTHELIUM DYSFUNCTION

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Background: APS is characterized by endothelium perturbation and hyperexpression of cellular adhesion molecule (CAM). In recent studies it was revealed that plasma levels of CAM were significant predictors of coronary artery disease in patients with inflammatory rheumatic diseases, but it has not been established whether increase level of CAM may be a marker of cardiovascular risk in APS. That is why the aim of this observation case was to investigate the link of sVCAM-1 concentration with disease activity and endothelium dysfunction as an early marker of atherosclerosis.

Methods: We studied 67 patients with APS: 21 (31.3%) with primary APS (PAPS), 19 (28.4%) with APS associated with systemic lupus erythematosus (APS-SLE), 27 (40.3%) with SLE without APS and 26 age and sex matched healthy controls (HC). All patients were subjected to complete clinical examination, disease activity and assessment for endothelium-dependent vasodilatation(EDVD) of brachial artery. Also plasma level of sVCAM-1 was evaluated by solid-phase assay in all patients.

Results: In patients with PAPS, APS-SLE and SLE without APS sVCAM-1 levels varied from 398 to 2727 ng/ml. The average level was 1404,9+-61,4 ng/ml, that was in 2,1 times higher than in HC. Increase level of test marker was revealed in 15 (71.4%) patients with PAPS, 13 (68.4%) APS-SLE and 20 (74%) SLE without APS. It was established positive correlation of increase sVCAM level with disease activity: with SLEDAI index ($r = 0{,}556$ $p < 0{,}05$), with C-reactive protein level ($r = 0{,}430$ $p < 0{,}05$) and ESR ($r = 0{,}345$ $p < 0{,}05$) and circulate immune complexes ($r = 0{,}345$, $p < 0{,}05$). No correlations were found with IgG isotype of antiphospholipid antibodies and anti-dsDNA antibodies. Patients with PAPS and APS-SLE with normal EDVD were associated with 1,5-fold increase of sVCAM-1 level, compared with HC and these groups with middle and high deviation of EDVD were associated with 1,8 and 2,4-fold increase of sVCAM-1 level respectively. Increase of sVCAM serum level positively correlated with decrease of EDVD

Conclusions: According to this data it might be hypothesized that increase sVCAM-1 level is a marker of endothelium dysfunction in patients with APS especially in presence of high disease activity.

Disclosure statement: All authors have declared no conflicts of interest.

VASCULITIS

344. PREVENTION OF TREATMENT-RELATED MORBIDITY IN ANCA-ASSOCIATED VASCULITIS: THE PATIENT'S PERSPECTIVE

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