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Antibodies Against Domain 1 and Domain 4/5 of β2 Glycoprotein I: Clinical Relevance in Obstetric Anti-Phospholipid Syndrome

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SESSION INFORMATION

Date: Monday, November 14, 2016

Session Title: Antiphospholipid Syndrome

Session Type: ACR Concurrent Abstract Session

Session Time: 2:30PM-4:00PM

Background/Purpose: The domain reactivity of antibodies against b2 glycoprotein I (anti-b2GPI) has been investigated in patients with thrombotic anti-phospholipid syndrome (APS), leading to the identification of antibodies targeting domain 1 of the molecule (anti-D1) as the most relevant autoantibody subpopulation. Scarce attention has been paid to the domain profiling of patients with pregnancy morbidity (PM). The aim of this study was to characterize the relevance of the fine epitope reactivity of anti-b2GPI antibodies in anti-phospholipid antibody (aPL)-associated PM.

Methods: Women with persistent positivity for anti-b2GPI IgG antibodies at medium-high titers, with at least one pregnancy and without systemic autoimmune disease were included. Anti-D1 and anti-D4/5 antibodies were tested using a chemiluminescent immunoassay and a research ELISA assay, respectively (QUANTA Flash b2GPI IgG and QUANTA Lite, Inova Diagnostics). Statistical analysis was performed using R package.

Results: 138 women fulfilling the inclusion criteria were retrospectively recruited at 3 referral

centres. 49 patients (35%) had obstetric APS, 18 (13%) thrombotic APS, 37 (27%) thrombotic and obstetric APS while 34 women (25%) were asymptomatic aPL carriers. 81 women (60%) displayed triple aPL positivity, 32 (23%) had two positive aPL test and 23 (17%) carried a single aPL positivity. 110 patients had at least one untreated pregnancy, culminating in a live birth in 31 cases (28%). 89 women underwent a pregnancy course while receiving treatment, with 71 women (80%) having a live birth. A significant difference in the distribution of positive anti-D1 antibodies emerged between women with or without PM and with or without thrombosis ($p=0.05$, $c^2=2.710$ and $p<0.001$, $c^2=12.174$, respectively); no significant difference was observed for anti-D4/5 antibodies (**Table 1**). In a multivariate logistic regression model also encompassing treatment, positive anti-D1 antibodies, but not anti-D4/5, were significantly associated with obstetric complications, conferring an odds ratio (OR) of 2.32 ($p=0.040$ and $p=0.724$, respectively). Triple aPL positivity corrected by treatment significantly predicted PM ($p=0.015$, OR=2.78).

Conclusion: Our data suggest that anti-D1 antibodies are significantly associated not only with thrombosis but also with obstetric morbidity while positive anti-D4/5 antibodies are not predictive of PM. **Table 1. Different combinations of reactivity against D1 and D4/5 in women with or without pregnancy morbidity (PM) according to the updated classification Criteria for APS and in women with or without thrombosis.**

	No PM (%)	PM (%)	No thrombosis (%)	Thrombosis (%)
Anti-D1+/anti-D4/5-	15 (29%)	43 (50%)	27 (33%)	31 (56%)
Anti-D1-/anti-D4/5+	9 (17%)	9 (11%)	16 (19%)	2 (4%)
Anti-D1+/anti-D4/5+	11 (21%)	14 (16%)	15 (18%)	13 (24%)
Anti-D1-/anti-D4/5-	17 (33%)	20 (23%)	25 (30%)	9 (16%)
Total	52	86	83	55

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