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SPECIAL ARTICLE

Avidity of anti-β2-glycoprotein I antibodies in patients with antiphospholipid syndrome

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Antibodies against β_2-glycoprotein I (anti-β_2GPI) are one of the hallmarks of the antiphospholipid syndrome (APS). However, they are heterogenic regarding their epitope specificity, pathogenic mechanisms and their avidity. In the current study we present some outstanding issues about avidity of anti-β_2GPI antibodies. Our results confirmed that high avidity anti-β_2GPI are associated with thrombosis and APS, while in low avidity anti-β_2GPI group non-APS (predominantly systemic lupus erythematosus) patients prevailed. *Lupus* (2012) **21,** 764–765.

Key words: anti-β_2-glycoprotein I antibodies; avidity; chaotropic test; thrombosis

Introduction

It was 15 years ago that Gharavi and Reiber suggested that high-avidity (HAv) autoantibodies could play a critical role in organ-specific autoimmune disorders, whereas in immune-complex-mediated disorders HAv and low-avidity (LAv) antibodies might be equally pathogenic.[1] According to Reddel and Krilis, clinical manifestations of antiphospholipid syndrome (APS) depend on several factors including antiphospholipid antibodies (aPL) avidity and aPL do not uniformly predict thrombosis.[2] Čučnik et al.[3,4] showed that HAv (better than LAv) antibodies against beta2-glycoprotein I (anti-β_2GPI) correlated with venous thrombosis in patients with APS. Therefore, the investigation was further extended as a multicentre study.

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Patients and methods

A total of 479 sera samples from patients with primary APS or APS associated with other autoimmune diseases and patients with positive anti-β_2GPI without APS were collected from 7 European centres. Positivity was confirmed for IgG anti-β_2GPI with the in-house anti-β_2GPI ELISA[5] in 226/479 sera samples (51 males, 175 females, mean age 40 years) and therefore were appropriate for further testing on avidity with chaotropic anti-β_2GPI ELISA. Increasing concentrations of NaCl were applied in the process of antibody binding.[5] When the binding at 0.5 M NaCl remained higher than 65% or below 25% of the binding at 0.150 M NaCl, the presence of HAv respectively LAv anti-β2GPI was established. Other samples were considered to be of heterogeneous avidity.[5]

Out of 226 patients, 166 met the revised Sydney clinical criteria for the diagnosis of APS:[6] 60 sera samples belonged to non-APS patients (56 with systemic lupus erythematosus [SLE]).[7] A total of 175/226 IgG anti-β_2GPI positive patients were

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Table 1 Distribution of clinical and laboratory features of patients with high- or low-avidity anti-β_2GPI antibodies

	High (No = 73)	*Low (No = 49)*	
Anti-β_2GPI Avidity	*No (%)*	*No (%)*	p
APS	64 (87.7)	30 (61.2)	<0.001
Non-APS	9 (12,3)	19 (64.7)	<0.001
Thrombosis:	55 (75.3)	27 (55)	=0.004
Arterial	18 (24.7)	16 (32.7)	NS
Venous	41 (56.2)	12 (24.5)	<0.001
Microvascular	2 (2.7)	7 (14.3)	<0.01
Obstetrical disorder	25/48 (52.1)	10/41 (24.4)	<0.005

anti-β_2GPI, antibodies against β_2-glycoprotein I; APS, antiphospholipid syndrome; NS, not significant.

females of whom 57 had APS-related obstetrical disorders.

Results

A total of 226 patients were divided into 3 categories: patients with predominantly HAv, predominantly LAv and heterogeneous anti-β_2GPI (73, 49 and 104, respectively). The distribution of clinical and laboratory features among APS and non-APS patients with HAv and LAv IgG anti-β_2GPI is shown in Table 1.

Discussion

Heterogenic avidity of anti-β_2GPI due to the nature of polyclonal response of antibodies is not rare. However, some patients have either majority of HAv or LAv anti-β_2GPI which was the basis of our approach. In this extended multicentre study, significantly more patients with APS were found in the group with HAv anti-β_2GPI compared with the group with LAv, while the opposite was true for patients with diseases without APS.[4,5,8] We also confirmed thrombosis, predominantly venous, as the main clinical feature associated with HAv anti-β_2GPI and a clear association of HAv anti-β_2GPI antibodies with obstetric complications. Higher pathogenicity of HAv anti-β_2GPI compared with LAv anti-β_2GPI was thus confirmed.

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