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Comparative Study between New Novel Biomarker Antiphosphatidylserine/ prothrombin Antibodies and Conventional Established Diagnostic Markers in the Lab Diagnosis of Antiphospholipid Syndrome

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Abstract

Background: Ant phosphatidylserine/prothrombin complex (aPS/PT) antibodies are emerging as an important marker in the lab diagnosis antiphospholipid syndrome (APS).

We aimed to compare performance of new novel marker aPS/PT antibody with that of conventional antiphospholipid antibodies (aPL) such as lupus anticoagulant (LA), anticardiolipin (aCL), and anti-β2-glycoprotein I (anti-β2GPI) in suspected APS patients. In this study we aimed to find the percentage of cases positive for aPS/PT antibodies in cases with bad obstetric history who had one or more antiphospholipid antibody positivity needed for diagnosis of APS. We further compared IgG and IgM component of aPS/PT with IgG and IgM components of aCL and anti-β2GP 1. Also,Cases which were positive for LA was also tested for aPS/PT to find the correlation.

Methods: Total 100 samples (registered for BOH panel) who fulfilled the lab criteria for diagnosis of APS were included in the study. IgG/IgM aCL, IgG/IgM anti-β2GPI and IgG/IgM aPS/PT were detected in serum using ELISA assay in Quantalyser 3000 (Inova, San Diego, CA, USA).

Lupus Anticoagulant was detected using Star Max (Diagnostica Stago, France).The two different coagulation tests used to detect Lupus anticoagulant (LA) were PTT-LA and dRVVT.

Results: Among 100 patients who fulfilled the lab criteria of APS having BOH included in our study showed 65% positivity for aPS/PT IgG/IgM.

Both IgG aPS/PT and aPS/PT IgM were seen in 60 cases out of 65.

Significant association were found on comparing the presence of aPS/ PT IgG with Cardiolipin IgG and aPS /PT IgM with Cardiolipin IgM ie 85% and 95% respectively

Also association was seen on comparing the presence of aPS/ PT IgM with Beta 2 glycoprotein IgM ie. 57% and significant correlation with Beta 2 Glycoprotein IgG ie 85%.

Out of 8 cases with LA positive result, 7(87.5%) were positive for aPS/PT, hence showing highly significant association.

Conclusion: aPS/PT antibody is closely associated with conventional antibodies of APS including LA. The determination of aPS/PT in clinical practice, in conjunction with that of other aPL, may improve the likelihood lab diagnosis of APS.

Introduction

The antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by thrombosis and/or pregnancy morbidity in the presence of persistently positive antiphospholipid (aPL) antibodies. The updated Sydney APS classification criteria include anticardiolipin antibodies (aCL), anti-β2glycoprotien-I (anti-β2GP-I) and lupus anticoagulant (LA) as part of the serological criteria [1].

The latest 2023 ACR/EULAR APS classification criteria include an entry criterion of at least one positive antiphospholipid antibody (aPL) test within 3years of identification of an aPL-associated clinical criterion, followed by additive weighted criteria (score range 1–7 points each) clustered into 6 clinical domains (macrovascular venous thromboembolism, macrovascular arterial thrombosis, microvascular, obstetric, cardiac valve, and hematologic)and 2 laboratory domains (lupus anticoagulant functional coagulation assays, and solid-phase enzyme-linked immunosorbent assays for IgG/IgM anti cardiolipin and/or IgG/IgM anti–β2-glycoprotein I antibodies). Patients accumulating at least 3 points each from the clinical and laboratory domains are classified as having APS[2].

aPL antibodies consist of family of other autoantibodies such as anti-phosphatidylserine/prothrombin (aPS/PT), anti-vimentin, anti-annexin, anti-phosphatidylethanolamine and antibodies directed against domain I of the β2GP-I molecule [3]. The inclusion of aPS/PT testing in the diagnostic workup of APS patients has been shown to add to the identification of individuals with APS [4]. Also, testing of aPS/PT testing and combining with other aPL testing, such as the concomitant positivity for LA, aβ_2GPI and aPS/PT tests,

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has been reported to be highly associated with the clinical features of APS patients, particularly vascular thrombosis, and obstetric complications [5]. Studies have demonstrated that the addition of aPS/PT improves risk stratification in APS [6].

Materials and Methods

Patient cohort

The present study was conducted in the Department of Haematlogy and Immunology, Dr. Lal Pathlabs, NRL over a period of 6 months.Total 100 samples (registered for BOH panel) which fulfilled the lab criteria for diagnosis of APS were included in the study. Age of patients ranged from 22-46 years. 67 patients were of age group 30-40, 26 of 20-30 age group and 7 patients above 40 years.

On the whole out of 100 pts - 54 patients were primipara and 46 were multipara.

Methods

Antibodies to phosphatidylserine-prothrombin (aPS/PT)

The presence of IgG/IgM aPS/PT were detected in serum using ELISA assay in Quantalyser 3000 (Inova, San Diego, CA, USA). The cut off values for IgG and IgM aPS/PT is >30 units.

Antibodies to cardiolipin (aCL) and β2- glycoprotein I (anti-β2GPI)

IgG/IgM aCL and IgG/IgM anti-β2GPI were detected in serum using ELISA assay in Quantalyser 3000 (Inova, San Diego, CA, USA). The cut off for IgG/IgM aCL is >20 GPL/MPL and for IgG/IgM anti-β2GP1>20 units.

Lupus anticoagulant (LAC)

LA was detected using Star Max (Diagnostica Stago, France). The two different coagulation tests used to detect Lupus anticoagulant (LA) were PTT-LA using Lupus anticoagulant sensitive APTT reagent and dilute Russell venom viper time (dRVVT). LA test was done with series of functional coagulation test. Both screening and confirming steps were performed. The LAC was considered positive if the normalized ratio ie. dRVVT screen ratio/ dRVVT confirm ratio is >1.20.

Results

Among these 100 patients with conventional antibodies and BOH, 65 patients were positive for aPS/PT IgG/IgM. Both IgG and IgM were seen in 60 cases out of 65.

We separately compared presence of aPS/PT IgG with aCL IgG and aβ2GP1 IgG and aPS/PT IgM with aCL IgM and aβ2GP1 IgM

aPS/ PT IgG vs Beta glycoprotein1 IgG =85%

aPS/ PT IgM vs Beta glycoprotein1 IgM =57%

aPS/ PT IgG vs Cardiolipin IgG=85%

aPS /PT IgM vs Cardiolipin IgM= 95%

Out of 8 cases with LA positive result 7(87.5%) were positive for aPS/PT.

aCL Ab		aβ2GP		LA	aCL + aβ2GP				aCL/ aβ2GP1 +LA	Total
35		12		5	45				3	100
IgM	IgG	IgM	IgG		aCL IgM	aCL IgG	aβ2GP IgM	aβ2GP IgG		
20	15	2	10		38	37	33	43		

Table 1: Following table shows the distribution of conventional antibodies in 100 cases of BOH included in study.
Among these 100 patients with conventional antibodies and BOH, 65 patients were positive for aPS/PT IgG/IgM. Both IgG and IgM were seen in 60 cases out of 65.

Discussion

This study was conducted to find the usefulness of aPS/PT antibody in the lab diagnosis of APS. We studied the correlation and percentage positivity of aPS/PT IgG/IgM in patients already having any 1 or more conventional antibody positivity along with clinical symptom of bad obstetric history.

aPS/PT have been widely investigated as an additional marker for APS. In a study conducted in France on the prevalence and significance of non-conventional Antiphospholipid antibodies in patients with clinical APS showed a high prevalence of IgG/IgM PS/PT antibodies. Prevalence of aPS/PT IgM was 65.8% and IgG was 43.9%.Further all patients who were positive for aβ2GP1 IgG were positive of aPS/PT [7]. In our study 65% positivity of aPS/PT was seen in patients with one clinical symptom and any 1 conventional antibodies. 85% patients who were positive for β2GP1 IgG were also positive for aPS/PT. In a Chinese study to determine the prevalence and clinical association of aPS/PT with thrombosis and pregnancy loss showed a positivity of 72% for aPS/PT IgG and 67.2% positivity for aPS/PT IgM. Both IgG and IgM were present in 53.2% patients [8]. In our study both IgG and IgM aPS/PT was found in 60% patients.

LA detection is important in case of thrombosis recurrence in patients undergoing treatment. LA detection method is not accurate for patients who are being treated with DOACs. Patients undergoing treatment with DOACs could give false positive result with dRVVT [9].In an article published by American College of Rheumatology showed most patients who were positive for IgG/IgM anti-PS/PT antibodies had LAC [10]. In our study out of 8 cases of LA positive patients 7 had aPS/PT. PS/PT antibodies testing is performed on serum sample by immunological assays and is not influenced by treatment of DOACs. Replacing LA testing or using in conjunction with aPS/PT in patients treated by DOACS need to be considered.

Conclusion

aPS/PT is closely associated with conventional antibodies of APS and LAC, and positive results from an aPS/PT test can mark thrombotic events in APS patients.

Further studies can be done to evaluate the use of aPS/PT as

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surrogate APS biological marker instead of LA to classify in high-risk profile patients treated by direct oral anticoagulants (DOACs), in whom LA detection cannot be achieved.

The determination of aPS/PT in clinical practice, in conjunction with that of other aPL, may improve the likelihood of recognizing APS.

References

1. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, et al. (2006) International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 4: 295-306.
2. Barbhaiya M, Zuily S, Naden R, Hendry A, Manneville F, et al. (2023) ACR/EULAR APS Classification Criteria Collaborators. 2023 ACR/EULAR antiphospholipid syndrome classification criteria. Ann Rheum Dis 82:1258-1270.
3. Uthman I, Godeau B, Taher A, Khamashta M (2008) The hematologic manifestations of the antiphospholipid syndrome Blood Rev 22: 187-194.
4. Bajaj SP, Rapaport SI, Fierer DS, Herbst KD, Schwartz DB (1983) A mechanism for the hypoprothrombinemia of the acquired hypoprothrombinemia-lupus anticoagulant syndrome. Blood 61: 684-692.
5. Roubey RA (1994) Autoantibodies to phospholipid-binding plasma proteins: a new view of lupus anticoagulants and other “antiphospholipid” autoantibodies. *Blood* 84: 2854-2867.
6. Noordermeer T, Chemlal S, Jansma JJ, van der Vegte V, Schutgens REG, et al. (2023) Anti-β2-glycoprotein I and anti-phosphatidylserine/prothrombin antibodies interfere with cleavage of factor V(a) by activated protein C. J Thromb Haemost 21: 2509-2518.
7. Litvinova E, Darnige L, Kirilovsky A, Burnel Y, de Luna G, et al. (2018) Dragon-Durey MA. Prevalence and Significance of Non-conventional Antiphospholipid Antibodies in Patients with Clinical APS Criteria. Front Immunol 9: 2971.
8. Shi H, Zheng H, Yin YF, Hu QY, Teng JL, et al. (2018) Antiphosphatidylserine/prothrombin antibodies (aPS/PT) as potential diagnostic markers and risk predictors of venous thrombosis and obstetric complications in antiphospholipid syndrome. Clin Chem Lab Med 56: 614-624.
9. Hoxha A, Banzato A, Ruffatti A, Pengo V (2017) Detection of lupus anticoagulant in the era of direct oral anticoagulants. Autoimmun Rev. 16: 173-178.
10. Nakamura H, Oku K, Amengual O, Ohmura K, Fujieda Y, et al. (2018) Kato M, Bohgaki T, Yasuda S, Atsumi T. First-Line, Non-Criterial Antiphospholipid Antibody Testing for the Diagnosis of Antiphospholipid Syndrome in Clinical Practice: A Combination of Anti-β_2 -Glycoprotein I Domain I and Anti-Phosphatidylserine/Prothrombin Complex Antibodies Tests. Arthritis Care Res (Hoboken) 70: 627-634.