Bahrain Medical Bulletin, Vol. 27, No. 2, June 2005

Anticardiolipin and anti-ß2-glycoprotein 1 in Omani patients with anti-phospholipid syndrome

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Objective: Anti-cardiolipin (ACA) and anti-ß2-glycoprotein I (ß2GP1) antibodies are thought to be involved in the development of arterial or venous thrombosis, thrombocytopenia and recurrent fetal loss. We examined the presence of these autoantibodies in Omani patients with autoimmune and non-autoimmune disorders.

Methods: Sera from 30 patients with systemic lupus erythematosus (SLE; 30), 44 with a history of recurrent abortion and 36 with thrombosis/thromboytopeania were tested for ACA and anti-ß2GP1 antibodies. In addition, sera from 30 healthy subjects were also tested for these antibodies.

Results: ACA were detected in 23% with SLE, 27% suffering from recurrent abortion and 36% of patients with thrombosis/thrombocytopenia while anti-ß2GP1 antibodies were detected in 16.6%, 18% and 22% of same patients, respectively.

Conclusions: Our data demonstrate a high prevalence of ACA and anti-ß2GP1 antibodies of either combined or separate pattern among the Omani patient groups studied.

Bahrain Med Bull 2005;27(2):

Anti-phospholipid antibodies are a heterogeneous group of immunoglobulins that bind to several anionic phospholipids, including cardiolipin[1,2]. High serum levels of ACA are frequently detected in patients with autoimmune (eg. SLE) and non-autoimmune diseases, as well as in apparently healthy individuals[3,4].

Studies have shown that plasma glycoprotein with phospholipid-binding property is required for ACA., to bind to cardiolipin that has been coated onto plastic plates. This cofactor has been identified as β2-glycoprotein 1 (β2GPl)[5,6]. Later, it was found that β2GPl is indeed the antigen to which many ACA patients are actually binding and the phospholipid merely serves to link the β2GPl to the solid phase[7].

Antibodies to cardiolipin and β2GPl have been associated with an increased risk for recurrent arterial and venous thrombotic events, thrombocytopenia and fetal loss. These manifestations are the main features of the anti-phospholipid syndrome (APS)[8-10]. The

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syndrome occurs in isolation (primary APS) or in association with connective tissue diseases (secondary APS), particularly SLE[11,12].

This study aimed to determine the prevalence of ACA and anti-β2GPl antibodies in sera from Omani subjects with SLE, thrombosis or thrombocytopenia and in women with recurrent abortion.

METHODS

Subjects

One hundred and ten serum samples from various patient groups (83 females and 27 males; mean age was 29 ± 11 years, range: 16-64 years) were analyzed to determine ACA and anti-β2GPl antibodies. In addition, serum from 30 healthy subjects of similar age and gender distributions were studied. Patient groups studied were diagnosed of having the following diseases (on the basis of the onset of signs, symptoms and other clinical and serologic abnormalities): SLE 30, a history of a recurrent pregnancy loss 44 and thrombosis/ thrombocytopenia 36.

RESULTS

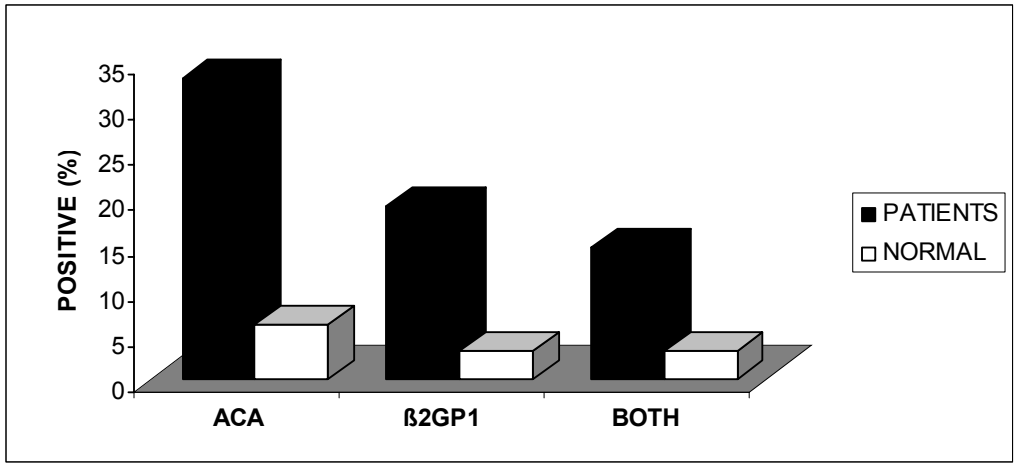

Figure 1. Prevalence of ACA and β2GPl in patients included in this study (n=110) and normal healthy control subjects (n=30)

Prevalence of ACA and anti-β2GP1 antibodies in both patients groups and normal subjects included in this study are shown in Figure 1 and Table 1. The percentages of positive sera for ACA and β2GP1 were 23% and 16.6% in the SLE group, 27% and 18% in the abortion group and 36% and 22% in the group with thrombosis/thrombocytopenia. In the normal healthy control group, the percentages of positive sera for ACA and anti-β2GP1 antibodies were found to be 6% and 3% respectively, with a significant difference when compared to the general picture in patients (33% and 19%).

Table 1. **Prevalence of ACA and β2GP1 in all patients groups as well as normal subject included in this study.**

	SLE (n=30)	ABORTION (n = 44)	THROMBOSIS (n=36)	NORMAL (n =30)
ACA	23%	27%	36%	6%
ß2GP1	16.6%	18%	22%	3%
BOTH	10%	13.6%	19.4%	3%

The percentage of patients who possessed serum ACA but no antibody to β2GP1 in each group was as follows: SLE (13%), abortion (13%) and thrombosis/ thrombocytopenia (16%). On the other hand, perecentages of subjects who tested positive for anti-β2GP1 antibodies only (negative for ACA) in each group was as follows: SLE 5%, abortion 2% and thrombosis/thrombocytopenia 3%.

Ten percent of sera from SLE patients were positive for both ACA and anti-β2GP1 antibodies, in the thrombosis/ thrombocytopenia group this was found to be 19.4% while in sera derived from women with history of a recurrent pregnancy loss 13% were positive for both antibodies. Among the normal healthy subjects included, 3% of the sera were also positive for both antibodies.

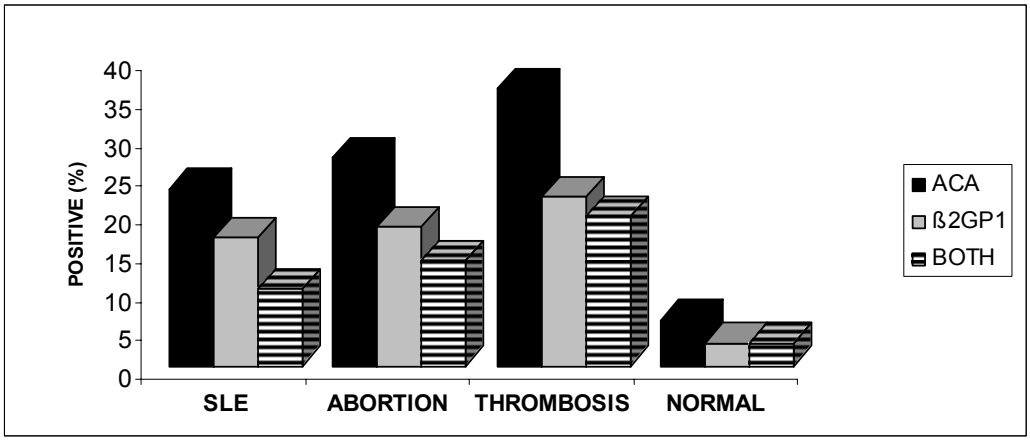

Figure 2. ACA and β2GP1 levels in sera from women with history of a recurrent pregnancy loss (n=44), patients with thrombosis/thrombocytopenia (n=36), with SLE disorder (n=30) as well as with normal healthy subjects (n=30)

DISCUSSION

ACA detects a heterogeneous group of antibodies with two distinct specificities: ß2GP1-dependent and ß2GP1-independent reactivity. Sera positive in ACA assay, but negative in ß2GP1-ELISA are found in patients with infectious diseases, and exhibited lower specificity and lower positive predictive value for APS clinical features[13,14]. In

contrast, patients whose sera were anti-ß2GP1 antibodies positive and ACA negative have been reported to have a high prevalence of clinical manifestations of APS[15].

Antiphospholipid antibodies are well-recognized factors in patients with SLE[16]. The present study confirms the high prevalence of antibodies to cardiolipin and ß2GP1 in patients with SLE (23% and 16.6% of SLE respectively). Furthermore, all SLE patients who tested positive for both ACA and anti-ß2GP1 antibodies had clinical manifestations of thrombosis or thrombocytopenia and, thus, were considered to be of a secondary APS type according to the classification established by Wilson et al[17] which applied to patients who had persistent elevated ACA together with the systemic autoimmune disease. The risk of thrombosis associated with antiphospholipid antibodies has been studied most thoroughly in populations with systemic lupus erythematosus, of whom 12%–30% had ACA[18].

The association between antiphospholipid antibodies and recurrent spontaneous abortion has also been documented[19,20]. Autoimmune ACA may induce pregnancy failure either by impairing embryonic implantation and/or binding directly to placenta[21,22].

An earlier study carried on Omani patients had shown that the presence of ACA was associated with the risk of abortions[23]. Our study confirmed the high presence of ACA and anti-ß2GP1 antibodies in sera derived from women with a history of recurrent abortion (27% and 18%, respectively). A previous group had reported ß2GP1 dependent ACA in 40% of the cases investigated[24]. This difference may be partly explained by variations in assay protocols of various laboratories used to detect ACA or due to the immune characteristics of this population compared to those analyzed by other authors[25]. Nevertheless, according to some reports, the frequency of ACA in recurrent pregnancy loss was found to range from 11% to 42%, which is closer to our findings[26,27].

ACA have been found to be strongly associated with increased risk of venous and arterial thrombosis and thrombocytopenia[28]. The current study showed a relatively high frequency of antiphospholipid antibodies in patients with thrombosis/ thrombocytopeania. A total of 36% of patients were positive for ACA, while 22% were positive for anti-ß2GP1 antibodies and 19.4% of these patients were positive for both antibodies. These results were in agreement with earlier reports on a similar group of patients[29,30].

One of the most difficult clinical issues in APS is the lack of specificity of ACA for the diagnosis, leading to the possibility of both false positive diagnoses and unnecessary anticoagulant therapy. An increase in clinical specificity may be achieved by testing both antibodies.

CONCLUSION

Our study confirms the presence of both antibodies (in various ratios) among the patients studied. It also demonstrates a specific pattern for both ACA and anti-ß2GP1 antibodies among the Omani patients studied. These are likely to contribute to the variation in results reported by different laboratories, particularly among those using the same assay.

Additional research is necessary to elucidate the relationship of the antibodies to the disease process, and to use this information towards improving diagnosis and treatment of affected patients.

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