

Antiphospholipid Antibodies in Neoplastic Patients

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Abstract

Background: Anti-phospholipid syndrome (APS) is an autoimmune systemic disease characterized by the persistent presence of anti-phospholipid antibodies (APA) and the occurrence of thrombotic events. Nowadays, the association between specific antibodies for anionic phospholipids with thrombotic events and other main clinical manifestations is well-recognized as "antiphospholipid syndrome". The present study was done to evaluate the frequency of antiphospholipid antibodies in neoplastic patients.

Material and methods: One hundred and eighty patients were included in this cross sectional study. Their suspected neoplasm disorders were confirmed by pathology or flowcytometry. History taking and clinical examination were done for patients to detect all symptomatic clinical thrombotic events. Antiphospholipid antibodies were tested for all patients.

Results: The study was concluded with 156 study samples. Thirty three patients (21.2%) had antiphospholipid antibodies. There was no significant difference on antiphospholipid antibodies frequency between two genders. APA frequency showed no significant difference between solid or non-solid tumors. The rate of thrombosis was significantly higher in neoplastic patients with antiphospholipid antibodies.

Conclusion: Frequency of antiphospholipid antibodies was significantly higher in neoplastic patients. Antiphospholipid antibodies were one of the multifactorial accelerating factors for thrombotic events in neoplastic patients.

Keywords: antiphospholipid antibody; thrombotic events; neoplastic patient

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Introduction

Anti-phospholipid syndrome (APS) is an autoimmune systemic disease characterized by the persistent presence of anti-phospholipid antibodies (APA) and the occurrence of thrombotic events. Anti-phospholipid antibodies are accepted, in the literature, as pathogenic antibodies which have direct effects against phospholipid-binding proteins. Induction of endothelial activation in both in vitro and in vivo experimental models was one of the suggested mechanisms for the pathogenesis of antiphospholipid syndrome. [1] Antiphospholipid syndrome is one of the various forms of antibody-mediated thrombosis. The mechanisms involved in the pathogenesis of these thrombotic events are discussed. [2]

Nowadays, the association between specific antibodies for anionic phospholipids with thrombotic events and main other clinical manifestations is well-recognized as "antiphospholipid syndrome" [3]. Various studies indicate that among the anti-phospholipid antibodies, LA is the most sensitive marker for APS while anti-beta(2)GPI IgG, aPT IgG,

and aPL IgG are risk factors for thrombosis [4]. The association between antiphospholipid antibodies with thrombosis in patients with antiphospholipid syndrome is well documented in humans and in animal studies. [5]

Antiphospholipid antibodies, due to thrombotic events, can be one of the first manifestations of malignancy. The pathologic significance of antiphospholipid antibodies in patients with malignancies, however, is still unclear. It is unclear whether the presence of antiphospholipid antibodies should be considered as the cause of malignancy or if it directly contributes to the development of thrombosis in these patients. In particular, solid tumors may be associated with the development of antiphospholipid antibodies, enhancing the thrombophilic risk in these patients. [6] The present study was designed to evaluate the prevalence of antiphospholipid antibodies in neoplastic patients.

Material and Methods

The present cross sectional study was approved by Yazd Medical University Ethical Board and was fully supported and funded by Yazd Medical University.

Table 1: APA status in our cases according to their age group

Group	Age		20 – 39 years		40 – 59 years		> 60 years		Total	
	< 20 years		N	%	N	%	N	%	N	%
Positive	1	16.7	12	27.3	15	24.6	5	11.1	33	21.2
Negative	5	83.3	32	72.7	46	75.4	40	88.9	123	78.8
Total	6	100	44	100	61	100	45	100	156	100

Results of table 1 shows that the frequency of APA was not significantly different among age groups ($P = 0.12$)

The present study evaluated APA prevalence in neoplastic patients.

Study samples

The study sample was comprised of 180 patients that were referred to Yazd oncology clinics between September 2006 and September 2007. Their neoplastic disorders were confirmed by pathology or flowcytometry. Sampling method was consecutive sampling. Age, sex, type of malignancy and type of thrombosis were our study variables. Information was collected by questionnaires, history taking, clinical examination and para clinical tests.

Study methods

History taking and clinical examination were done for all cases to detect all cases of symptomatic clinical thrombosis. Patients without thrombosis were followed up for 6 months. Antiphospholipid antibodies (APS) were evaluated for all our patients. Anti phospholipid antibodies (IgG & IgM) were assessed using ELIZA immunoassay (EIA) with ORG529 Kit. Antibodies titers higher than 10U/ml were labeled as positive results. Cases, were divided to positive and negative APA according to APA results and were evaluated for the frequency and time of clinical thrombosis.

Statistical analysis

Data analysis was done with SPSS software Version 14.0 (SPSS Inc, Chicago Ill). Chi square test was used for evaluating APA results in our cases according to their age groups, sex and type of tumor. Mann-Whitney test was used for comparing time of thrombosis in the two groups. A P value less than 0.5 was considered significant.

Results

In the beginning of the study, 139 patients had APA negative results and 41 patients had APA positive results. 11 patients died during the study period and 9 patients refused to collaborate. Four patients had positive results in the second APA test although their primary APA test was negative. All these cases (24 patients) were excluded from the study.

The study ended with 156 cases. Mean of age in our patients was 48.25 ± 17.26 years old. Cases were divided to 4 age groups: younger than 20, 20

– 39, 40 – 59 and older than 60 years. Eighty patients (51.3%) were female. One hundred and five patients had a solid tumor.

Thirty three patients (21.2%) had positive results for APA test. In our cases, 51 patients (32.7%) had clinical thrombosis. Frequency of APA did not show a significant difference among age groups ($P = 0.12$). All details are presented in Table 1.

Mean of age in positive APA group was not significantly different in comparison to mean of age in cases with negative APA results (45.27 ± 18.19 vs 49.04 ± 16.98 , P value = 0.27) Positive APA results were seen in 15.8% of men and 26.3% of women. There was no significant difference between two genders. ($P = 0.08$)

Table 2: APA status in our cases according to gender

Group	Sex		Female		Total
	Male		N	%	
Positive	12	15.8	21	26.3	33
Negative	64	84.2	59	73.8	123
Total	76	100	80	100	156

Results of table 2 shows that there was no significant difference between genders. ($P = 0.08$)

21 (20%) patients with a solid tumor had positive APA results while 84 patients (80%) were negative for APA. From 51 patients with Non – solid tumors, 12 patients were positive for APA while 39 patients (76.5%) were negative. On the other hand, APA prevalence was not significantly different between cases with solid or non solid tumors. ($P = 0.38$)

Table 3: APA status in our cases according to type of tumor

Group	Sex		Non - solid		Total
	Solid		N	%	
Positive	21	20	12	23.5	33
Negative	84	80	39	76.5	123
Total	105	100	51	100	156

Results of table 3 shows that APA prevalence was not significantly different between solid or non solid tumors. ($P = 0.38$)

In positive cases for APA, 20 patients (60.60%) and in patients negative for APA, 31 patients (22.30%) had clinical thrombosis ($P = 0.00$). Rate of thrombosis was significantly higher in patients with malignant disorders ($P = 0.00$, $RR = 2.40$).

Overall, 51 thromboembolic events happened in our study. Twenty seven of them were deep vein thrombosis, 14 were hand superficial veins thrombosis, 2 were portal vein thrombosis, 3 were iliac and femur vein thrombosis, 2 of them were extended thrombosis of portal vein, splenic, mesentery and pulmonary veins and 3 of them had pulmonary emboli. The present study showed that time of thrombosis was lower in patients with APA. Mean duration between thrombosis and diagnosis of malignancy was 3 months in patients with APA and 8 months in patients without APA ($P = 0.01$).

Discussion

The present study was done to determine the prevalence of APA in neoplastic patients and assess its frequency according to their age, sex and tumor type. We aimed to evaluate the relationship between APA and clinical idiopathic thrombosis in patients with malignant disorders. Frequency of APA in our cases was 21.2% which was similar to reports of other studies [7-10]. In contrast to our results, some studies have reported these rates to be 30% or 41% in non Hodgkin lymphoma (NHL). Moreover, they have failed to find a relationship between APA and age, sex or disease severity [11, 12]. Although the relationship between APA and thrombosis has been clearly established, some studies have failed to show it [7-10].

It is estimated that the frequency of thromboemboly is more than 11% and is more prevalent in patients with specific malignancies in some organs such as pancreas, lung, urinary ducts, abdomen and breast [13]. Thromboembolic events can be predictive of cancer in the next years [14, 15]. However, some studies have reported little importance for the relationship between cancer and thrombotic events [16]. Risk of cancer increases in patients with pulmonary emboli or deep vein thrombosis [17, 18]. Early detection of thrombosis can help us to diagnose malignancies in some patients.

According to literature, antiphospholipid antibodies have been accepted as one of the causes of thrombotic events. On the other hand, the relationship between cancer and antiphospholipid antibodies has been shown in several studies [19, 20] although some studies have failed to report any

relationship between APA and thrombotic events [7-10].

Our study had some limitations. First, we had time and case limitation and were not able to perform our study specifically on selected neoplasms. Second, the study was restricted to an Iranian population and third, it was conducted in a single center and therefore external generalizability of our findings to other countries or centers is not possible.

Conclusion

APA frequency was significantly higher in patients with malignant disorders. There is no significant relationship between APA in patients with malignant disorders with their age, sex or type of tumor.

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