LETTER TO THE EDITOR

Frequency of Antiphospholipid Antibodies in Iranian Patients with Solid Malignancies: A Pilot Study

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Antiphospholipid antibodies (aPLs) are a family of immunoglobulins acting against different phospholipids or their complexes with plasma proteins. Included in this family are lupus anticoagulant (LA), antibodies to cardiolipin antibodies (aCLA) and to beta2 glycoprotein I (aβ2GP1). Some clinical manifestations associated with aPLs are venous and arterial thromboses, thrombocytopenia, hemolytic anemia, obstetric complications as recurrent spontaneous abortion, and livedo reticularis (1).

APLs are reported in patients with hematological malignancies and solid tumors such as β-cell lymphoma, non–Hodgkin's lymphoma (NHL), chronic myeloid leukemia (CML), renal cell carcinoma, melanoma and lung cancer (2). Previous studies have shown that aPLs increase in cancer patients and this may be a contributing factor to the increased incidence of thromboembolism events like venous thrombosis and pulmonary embolism in these patients which in turn is associated with poor prognosis (3). That is why some suggest that aPLs may be considered as markers for disease activity and progression in certain malignancies because of their effects on mortality and morbidity during the course of cancer (4). On the other hand, some authors suggest increased prevalence of certain cancers in patients with aPLs (5). Other studies showed no relation between aPLs and certain cancers (6).

It seems that aPLs are important factors to study in cancer patients. Therefore we studied a group of Iranian patients with different types of malignancies to measure aPL titers and to evaluate possible association with malignancies.

52 patients including 20 males and 32 females with different types of solid malignancies were randomly enrolled from Nemazee Hospital, Southern Iran, during their routine follow up from June 2006 to May 2007. Sera were prepared and stored at -20°C until analysed.

Keywords: Antiphospholipid Antibody, Leukemia, Lymphoma

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The patients age ranged from 3 months to 74 years (29.33 ± 22.19) and all were afflicted by some kind of cancer, including malignancy of: soft tissue, 6 males (11.5%), 4 females (7.7%); bone, 2 males (3.84%), 2 females (3.84%); urinary system, 0 male (0%), 2 females (3.84%); CNS, 4 males (7.7%), 5 females (9.6%); breast, 0 male (0%), 11 females (21.1 %); acute leukemia, 2 male (3.84%), 4 females (7.7%); lung, 2 males (3.84%), 1 female (1.9%); liver, 1 male (1.9%), 0 female (0%); digestive system, 2 males (3.84%), 2 females (3.84%); reproductive system, 0 male (0%), 2 females (3.84%).

History and physical exam of all patients showed no evidence of thrombosis. Blood samples from the patients were sent to A. Bianchi Bonomi Hemophilia and Thrombosis Center in Milan, Italy, to measure aCLAs (IgG and IgM) and aβ2GP1 (IgG and IgM) using Enzyme-Linked Immunosorbent Assay (ELISA) technique. The values obtained were as follows: aCLA IgG < 10 GPL, aCLA IgM < 10 MPL, aβ2GP1 IgG < 0.130 optical density (OD) and aβ2GP1 IgM < 0.280 (7). None of the patients showed positive IgG and IgM aCLA titers (1.16 ± 1.9 and 0.19 ± 0.44, respectively). Furthermore, values of IgG and IgM aβ2GP1 were within normal limits (0.1 ± 0.01 and 0.18 ± 0.13, respectively) in all excluding one female with breast cancer and lung metastasis who was found to be positive.

Although the association of aPL and malignancy has repeatedly been investigated in previous studies, but there are still many controversial issues regarding its first manifestation, risk of thrombosis, prognosis and pathogenicity. Gomez-Puerta et al have shown that particularly in elderly patients, the thrombotic events are associated with aPL and can be the first manifestation of malignancy (8). At the same time, the presence of aPL in patients with malignancies has important implications in their treatment and prognosis (8). Scorbohaci ML, indicated that in patients with malignancy, the prevalence of aPLs increased the risk of thrombosis (9). The underlying mechanism responsible for thromboembolism in patients with aPLs is due to an acquired resistance to activated protein C (APC) following interactions among aβ2GP1, prothrombin-binding antibodies and the protein C system. aβ2GP1 is the principal target antigen for antiphospholipid antibodies in patients with antiphospholipid antibodies. It binds with high affinity to atherogenic lipoprotein Lp (a) which shares structural homology with plasminogen, a key molecule in fibrinolytic system, and a possible endogenous regulator of fibrinolysis. Thus, an impairment of aβ2GP1-stimulated fibrinolysis by aβ2GP1 may be involved in the development of thrombosis in patients with anti-phospholipid syndrome (APS) (10). Grossman et al highlighted the importance of malignancy work in patients with severe digital ischemia associated with APS (11). On the contrary, Zimmerman-Gorska et al did not observe a difference in aPLs prevalence between a group of patients with breast cancer and the controls (6). Moreover, Miesbach et al found that high titres of IgM-antiphospholipid antibodies are unrelated to pathogenicity in patients with non-Hodgkin's lymphoma. Other studies have shown that there is no correlation between malignancy and its manifestations with aPLs (12).

Thus, the current study was conducted to investigate the relationship between aPLs and solid malignancy in Iranian patients as the prevalence of aPLs in this group could be an additional risk factor for thrombosis. To best of our knowledge, this is the first study performed on Iranian patients with solid malignancy and our results support the idea that there is no significant association between aPLs and solid malignancies. Our study considered the frequency of aPLs in cancer patients and we did not have a control group. Further studies are still required to fairly clarify this subject.

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