CORRESPONDENCE

Apoptotic Antigens, B₂-Glycoprotein I, and Antiphospholipid Autoantibodies

To the Editor:

We read with interest Silvestris et al.'s article describing a correlation between antibodies to phosphatidylserine (PS) and T-cell apoptosis in human immunodeficiency virus (HIV)-positive patients. They suggested that this could explain the increased generation of nonpathogenic IgG to acidic cell membrane phospholipids that are externalized during the enhanced lymphocytic apoptosis in HIV infection. The synthesis of IgG anti-PS as a byproduct of T-cell apoptosis would then account for the absence of thrombophilia.

Independently, we have recently proposed a similar apoptotic mechanism to partially attribute the presence of the subpopulation of naturally-occurring antiphospholipid (aPL) antibodies in healthy individuals. Our view followed from the in vivo studies of Chonn et al. that strongly indicated that B₂-glycoprotein I (B₂-GPI), a PL-binding plasma protein, plays an essential role in mediating the immunophysiologic clearance of senescent cells by binding to PS on the apoptotic cells. This complex of the aPL cofactor, B₂-GPI with anionic PL on apoptotic membranes would induce immunogenic epitopes that then stimulate the production of natural aPL.

Interestingly, Emlen et al. who previously reported an elevated level of lymphocytic apoptosis in SLE patients has observed that the binding of aPL to apoptotic SLE lymphocytes are B₂-GPI-dependent (personal communication, August 1996). Emlen et al. further commented that in SLE, the majority of the apoptotic activity may involve activated B cells. This thus raised the question regarding the differential genesis of harmful and benign apoptosis-derived aPL in SLE and HIV patients as well as normal subjects, respectively.

Perhaps, with regards to SLE and HIV infection, one reason may be related to evidence indicating that the mechanism of T cell and B cell apoptosis could proceed through fundamentally dissimilar pathways. By extension, this might lead to the release of different potential cytosolic and nucleolar antigens. Whether this has any significant influence or the pathogenicity of the activated aPL remains to be determined. Alternatively, during apoptosis, the different functional roles of B₂-GPI and other PL-binding proteins including eg, prothrombin, histones in modulating phospholipid antigenicity might explain the varying specificity of aPL in normal, infectious and autoimmune sera.

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REFERENCES

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