

Monday, July 13, 1981

Poster Presentations

Coagulation – III

11:00–12:30 h

Kenora Room Boards 113–124

0090

LUPUS-LIKE ANTICOAGULANT IN A PATIENT WITH SEVERE FACTOR VIII DEFICIENCY. R.S. Weinger, J.L. Moake, D. Deykin, A. Lopez, J.D. Olson. Medical Service, Boston VA Medical Center, Boston, MA., and Department of Pathology, University of Texas Medical School, Houston, Texas, U.S.A.

A severe hemophiliac (<1% FVIII-AHG) was transfused with FVIII concentrate and had orthopedic surgery without complication. His *in vivo* FVIII-AHG survival was normal ($T_{1/2}$ = 8hrs), as was his fibrinogen level, prothrombin (PT) and thrombin times. His prolonged (>100 sec.) activated partial thromboplastin time was incompletely corrected (40 sec.; normal <36 sec.) by the *in vitro* addition of an equal volume of pooled normal plasma, and did not become further prolonged after 1/2 and 2 hr. incubations at 37°C. A specific inhibitor to FVIII-AHG was not present. However, a thromboplastin inhibition test using patient plasma and progressively higher dilutions of rabbit brain thromboplastin (whole phospholipoprotein membranes) in a PT test system was positive. When either normal gel-separated platelets (GSP) or a dilute suspension of inosithin was used as a source of phospholipid, and clotting then initiated by the simultaneous addition of calcium and Russell's viper venom (to activate FX directly), patient plasma clotting times were similar to the clotting times of normal plasma and other severe FVIII-AHG deficient plasmas. In contrast, when both normal GSP and dilutions of tissue thromboplastin reagent were added to plasma, and clotting then initiated by recalcification, patient plasma clotting time was prolonged in comparison to the clotting times of normal plasma and other FVIII-AHG deficient plasmas. This "lupus-like" anticoagulant had no effect on *in vivo* hemostasis, even in our patient with severe hemophilia A. The anticoagulant differs from a lupus anticoagulant recently well characterized (Thiagarajan et al., J.Clin.Invest. 66:397,1980) in that it interacts better with phospholipoprotein membranes than with free phospholipids, and the *in vitro* defect is not corrected by the addition of normal platelets.

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ISOFOCUSING USED TO STUDY THE SPECIFICITY OF THE "LUPUS INHIBITOR". M.C. Coots, H.I. Glueck, M.A. Miller. Department of Pathology and Laboratory Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA.

This work was undertaken to investigate the clotting factor inhibition of the "lupus inhibitor". Thiagarajan and Shapiro (Circulation 62: 279, 1980) showed that the "lupus anticoagulant" had immunologic specificity for the negatively charged phospholipids. However, in various case reports specific clotting factor inhibition has been described.

In our studies, the adsorbed, heat defibrinated (56°C, 30 min.) plasmas of 6 patients with the "lupus inhibitor" were separated by preparative isofocusing. The inhibitory peaks were identified, and the clotting factor specificity of each was determined using partially purified eluates and specific factor deficient plasmas. The inhibitory peaks had activity against factors X, XI and XII in 5 of the 6 patients. In 1 patient, activity was confined to factor XI. These findings verified the initial factor quantitations. Utilizing the sequential Russell's viper venom time, X-X_a was inhibited to a greater degree than the factor V and the phospholipid in the formation of prothrombinase. The celite eluate inhibition test (for XI, XII inhibition) was abnormal in all six patients.

Based on this study, the lupus inhibitor in these six patients was a heterogeneous collection of inhibitors directed against factors XII, XI and X rather than a homogeneous entity.