FREE COMMUNICATIONS VIII

Coagulation: Factor VIII—Von Willebrand Protein, Structural Aspects

vWF II, A NEW VON WILLEBRAND’S DISEASE ANTIGEN, R.R. Montgomery and T.S. Zimmerman, Scripps Clinic and Research Foundation, La Jolla, California, U.S.A.

Factor VIII-related antigen (vWF II) is a protein of high molecular weight which co-purifies with Factor VIII procoagulant activity and von Willebrand factor under a variety of conditions. It is decreased or absent in most cases of von Willebrand's disease (VWD). We now report the existence of a second antigen (vWF III) which is absent from the plasma of individuals (8/3) with severe VWD but present in normal amounts in the plasma of individuals (8/8) with moderate or variant VWD. vWF III is present in normal platelets and is released from them during clotting. However, it is also present in platelet-free plasma from normal individuals which has been collected in a variety of protease inhibitors including benzamidine, hirudin, Trasylol, PMSF and soybean trypsin inhibitor suggesting that it circulates in plasma in vivo. The plasma from a patient with intravascular coagulation was found to have increased vWF III.

vWF II is defined by antibodies raised against void volume fractions of American Red Cross Factor VIII concentrates subjected to agarose gel chromatography. Antibodies raised against highly purified vWF II do not detect vWF III. Cross immunoelectrophoretic analysis shows vWF III to have a more anodic mobility than vWF II. vWF III exhibits no immunologic cross-reactivity with vWF II nor with vWF II fragments produced by plasmin, a-chymotrypsin, trypsin or elastase. Though the absence of both antigens from the plasma of individuals with severe VWD suggests a biologic linkage, immunologic evidence for the origin of these two species from a common precursor has not been demonstrated.


We have previously shown that patients with severe von Willebrand’s disease (VWD), mainly homozygotes, had no factor VIII related antigen (F VIII) in their platelets as well as no von Willebrand activity (F VIII:Ag) as measured by the ristocetin cofactor assay. In all other patients with less severe forms of the disease platelet F VIII:Ag was detectable. In normal controls electrophoretic mobility of platelet F VIII:Ag was found to be identical to the mobility of plasma F VIII:Ag either on the total platelet lysate or after isolation on agarose 40 columns. In the present study F VIII:Ag and the electrophoretic mobility of F VIII:Ag were compared in platelet extracts and the plasma of a number of patients. Seven of the ten patients tested were genetic variants of VWD with very low ratio of F VIII:Ag suggesting a non-functional protein with an increased electrophoretic mobility. One group of patients showed abnormalities of platelet F VIII:Ag identical to those found in the plasma. However another group showed a high ratio of F VIII:Ag suggesting a more active protein than the one in patient’s plasma although the F VIII:Ag platelet F VIII:Ag had an increased electrophoretic mobility. These results are the first example of F VIII:Ag with abnormal electrophoretic mobility associated to high F VIII:Ag activity. The loss of F VIII:Ag in the patient’s plasma would be a secondary process occurring after F VIII:Ag is released in the circulation.