497

A NEW VARIANT OF FACTOR X DEFICIENCY (FACTOR X ROMA).
V. De Stefano, G. Leone, R. Ferrelli, B. Bizzi. Istituto di Semeiotica Medica, Università Cattolica, Roma, Italy.

A 13 years-old-girl was admitted in our Hospital for a large muscle hematoma of left psoas. At age 3 she had a severe tonsillar bleeding following angina. Afterwards she suffered from easy bruisability and recurrent epistaxis. Prothrombin time (PT) was slightly prolonged (14.7 sec, control 12 sec, INR 1.5), while a more marked prolongation in aPTT was noticed (54.7 sec, control 30.3 sec). All clotting factors resulted within the normal range but Factor X. Factor X antigen was 0.95 U/ml (Laurell), whereas Factor X activity was 0.52 U/ml by extrinsic system assay (rabbit brain and lung thromboplastin), 0.06 U/ml by intrinsic system assay (rabbit brain cephalin) and 1.15 U/ml by activation by RVV-cephalin. Chromogenic assays (S-2222 and CBS 3139) performed after activation with RVV gave 1.02 U/ml and 1.00 U/ml, respectively. The patient plasma had no inhibitory activity against Factor X. The parents of the proposita (first cousins) had Factor X antigen levels and RVV functional activity around 1.00 U/ml, whereas Factor X activity tested by extrinsic and intrinsic system assay was about 0.60 U/ml and 0.50 U/ml, respectively. This Factor X variant seems different from the other ones previously described, showing normal antigen levels and RVV activation, a severe defect in the intrinsic activation and only a partial defect in the extrinsic activation. In particular the two defects more close to it (Factor X Friuli and Factor X Melbourne), both found in patients with Italian ancestry, were different because of a very prolonged PT (Factor X Friuli) or a normal PT (Factor X Melbourne).

498

INVOLVEMENT OF FACTOR XII (F XII) AND PREKALLIKREIN (PKK) IN THE ACTIVATION OF UROKINASE (UK)-RELATED PROTEINS IN HUMAN PLASMA.
D.J. Binnema and G. Dooijewaard. Gaubius Institute TNO, Leiden, the Netherlands.

Recently it has been shown that in human plasma two types of UK-related proteins occur: Type I, plasma UK, with UK-related antigenic determinants directly accessible to anti-UK antibodies and Type II with UK-related antigenic determinants which become accessible only after SDS treatment and separation of polypeptides on PAGE. In this study we compared the molecular and enzymic properties of the two types in: 1. plasma activated by dextran sulphate (DXS) euglobulin precipitation, 2. plasma that was not activated and 3. plasma deficient in F XII, depleted in PKK and subsequently activated by DXS. ACA 34 gel chromatography, SDS PAGE, fibrin underlay zymography and immunoblotting were used. Results:

Treatment of plasma	Type	Molecular Weight whole molecule	Molecular Weight UK-related subunit	Condition UK-related subunit	Spec. act. (IU/µg)
DXS	I	150,000	55,000	cleaved	100
	II	500,000	110,000	cleaved, UK antigen on 37kD polypeptide	<10
none	I	55,000	55,000	single chain	< 1
	II	650,000	110,000	single chain	< 1
-FXII, -PKK, +DXS	I	55,000 / 150,000	55,000	cleaved	100
			55,000	cleaved	100
	II	500,000	110,000	single chain	< 1

Conclusions: 1. The UK-related subunits of TI and TII are active when cleaved, but relatively inactive in the single-chain form. 2. The presence of F XII and PKK is indispensable for activation of TII, but not for that of TI; TII contributes to the F XII-dependent plasminogen activator activity reported earlier, TI to the F XII-independent part. 3. Activation of TI by DXS with no F XII and PKK present impairs the formation of the 150,000 form. 4. The specific activity of TII is rather low, but its concentration in plasma (not shown) is at least ten times that of TI.

499

REDUCED ß-FXIIa-INHIBITION CAPACITY IN HEPARINIZED PLASMA SAMPLES.
G. Fuhrer, M.J. Gallimore, W. Heller and H.E. Hoffmeister. Department of Cardiovascular Surgery, University of Tübingen, FRG

It has been shown by our group that ß-FXIIa-inhibition was reduced in platelet rich plasma. To investigate the effect of heparin on ß-FXIIa-inhibition, kallikrein inhibition and C1-esterase inhibition high and low molecular weight heparin preparations were added to plasma samples. Using high molecular weight heparin from 0 to 5 anti Xa/ml a reduction in ß-FXIIa-inhibition was seen from 103% to 59%.These effects were abolished by the addition of protamine chloride. No changes of kallikrein inhibition and C1-esterase-inhibition were observed in heparinized plasma samples. After the addition of a low molecular heparin preparation to plasma samples, the reduction of ß-FXIIa-inhibition was markedly decreased. The levels of the Hageman fragment inhibitor capacity were lowered to 22% compared to initial values of 91%. The antagonization of heparin normalized these values. No reduction in kallikrein inhibition and C1-esterase inhibition were found in these samples because in all three assays C1-inhibitor activity is analysed, purified C1-inhibitor was added to buffer containing several heparin concentration (see table)

	0	0,5	1,0	2,0	3,0 heparin/ml
ß-FXIIa inhibition	107	100	96	76	72 %
kallikrein inhibition	105	107	109	100	106 %
C1-esterase inhibition	123	122	126	127	127 %

These results suggest that the inhibition of ß-FXIIa is markedly affected by heparin whilst no changes were seen in the inhibition capacity for C1-esterase and kallikrein.