

RECURRENT VENOUS THROMBOSIS RELATED TO A HEREDITARY DYS-FIBRINOGEN WITH ABNORMAL CROSSED IMMUNOELECTROPHORETIC PATTERN. A.C. Papp, R.M. Snopko, E.R. Cole, R.J. Sassetti and K.K. Wu. Section of Hematology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL U.S.A.

A 24 year old man with a history of multiple recurrent venous thrombosis was found to have a qualitatively abnormal fibrinogen. Plasma fibrinogen concentration by a kinetic thrombin time method was 135mg% as compared to 150mg% by the gravimetric method of Ratnoff and Menzie. The thrombin, reptilase and Russell viper venom times were all approximately 50% longer than the normal values. Neither the thrombin time nor reptilase time was corrected upon addition of  $\text{CaCl}_2$ . Antigenic quantitation by Laurell immunoelectrophoresis gave a value of 320mg%. On Ouchterlony immunodiffusion plate, the patient's plasma and normal plasma showed a line of identity. The patient's fibrinogen had a normal rate of migration by one-dimensional immunoelectrophoresis but it exhibited an abnormal pattern upon crossed immunoelectrophoresis. The abnormality is characterized by the presence of a shoulder on the anodal side of the fibrinogen peak. Family studies revealed that the fibrinogen defect was inherited as an autosomal dominant trait. To determine whether recurrent venous thrombosis is related to increased viscosity due to the abnormal fibrinogen, fibrinogen was purified by the method of Blombäck and the relative viscosity of fibrinogen solution was determined. Preliminary data were suggestive of an increased viscosity of the patient's fibrinogen. These findings indicate that the immunologically abnormal dysfibrinogen may be responsible for recurrent venous thrombosis because of alteration of the physico-chemical properties of the fibrinogen molecule.

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FIBRINOGEN CONSUMPTION IN BREAST CANCER AND ITS RELATION TO THE EXTENT AND TYPE OF METASTASES. V. Pengo, G. Cartei, D. Casara, C. Guerra, E. Bertaglia, R. Zanella, M. Bajo, P. Belmonte. Clinica Medica I Università di Padova, Divisione di Oncologia Medica - Divisione di Radioterapia Ospedale Civile di Padova, Padova, Italy.

A subclinical intravascular coagulation-fibrinolysis syndrome (I.C.F.), is commonly present in cancer patients: a shortened fibrinogen half-life, in fact, have been found in most patients with malignancies, not considering, however, the type and extent of disease. 28 breast cancer patients, without bleeding and thromboembolic disorders and not receiving chemo-radiotherapy, have been assessed for the presence of I.C.F. syndrome by mean of radiofibrinogen half-life, fibrinogen level, ethanol gelation test, fibrinogen/fibrin degradation products (FDP). 16 patients without metastases were studied before surgery, while 12 patients with metastases were studied after more than one month from the operation (7 diffuse metastases, 5 pulmonary metastases). 14 out of 16 patients of the first group, and 6 out of 7 with diffuse metastases showed a markedly shortened fibrinogen half-life (hours) ( $\bar{x}=53.9 \pm 18.2$ ,  $\bar{x}=54.2 \pm 16.4$  as mean  $\pm$  SD respectively), while all the patients with pulmonary metastases showed a normal fibrinogen half-life ( $\bar{x}=84 \pm 9.9$ ). Normal range was 73-91 h. FDP were almost always normal. In conclusion the tumor per se determine a fibrinogen consumption without a competent fibrinolysis. Pulmonary metastases don't promote fibrinogen consumption and/or they don't need fibrin for their growth and spread.

FUNCTIONAL AND BIOCHEMICAL STUDIES ON A CASE OF DYSFIBRINOGENEMIA (FIBRINOGEN GENOVA). H.J. Hassan, M. Orlando, P. G. Mori, G. Tonini, P. Casalbore, A. Sarti, E. Boeri and L. Tentori. Laboratorio di Patologia non Infettiva, Istituto Superiore di Sanità, Rome, Italy. Istituto G. Gaslini, Genova Quarto, Italy.

Fibrinogen Genova was recognized in an Italian family. The propositus had no bleeding tendency and diagnosis was performed on the basis of prolonged prothrombin, thrombin and reptilase times of plasma, associated with normal fibrinogen levels. The purified fibrinogen showed an inhibitory effect on the clotting times of the normal one.

Functional studies performed on purified fibrinogen revealed that the clottability was reduced (74%, normal 88-94%) and the thrombin polymerization curve was abnormal due to a delayed fibrin monomers aggregation. The fibrinopeptides release was normal.

Analysis of plasmic derivatives carried out by both SDS gel electrophoresis (5 and 9%) and immunological methods showed some differences compared with normal fibrinogen. The fibrinogen chains were studied on isoelectric focusing slabs and SDS gel electrophoresis. Preliminary results did not reveal any difference with normal.

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EASMA FIBRINOPEPTIDE A AND  $\beta$ -THROMBOGLOBULIN IN THE PATIENTS WITH THROMBOTIC DISORDERS. T. Murakoshi, H. Takei, T. Seya, Y. Oguma, M. Yamauchi, H. Nagata and H. Hasegawa. First Department of Internal Medicine, Hokkaido University School of Medicine, Sapporo, Hokkaido, JAPAN.

Fibrinopeptide A (FPA) is a sensitive indicator of the thrombin action and  $\beta$ -thromboglobulin ( $\beta$ -TG) is a useful marker of the platelet activation. In order to know the coagulation disturbances in thrombotic disorders, the measurement of the two indicators is very important. However, relationship between these two indicators is not well studied. We measured plasma FPA and  $\beta$ -TG levels in the patients with decompensated DIC, lung cancer, gastric cancer, leukemia, thrombosis, and ARDS. In addition, influences of heparin and urokinase on plasma FPA and  $\beta$ -TG levels were investigated. Plasma FPA and  $\beta$ -TG levels were elevated in decompensated DIC (mean FPA: 14.0 ng/ml, mean  $\beta$ -TG: 73.9 ng/ml), but in some cases, these two indicators didn't change in the same manner. This difference was thought to be due to the concentration of plasma fibrinogen and a number of platelets. In the patients with lung cancer, elevated FPA and  $\beta$ -TG levels were found, and the former was elevated with progress of clinical stage. In some patients with leukemia, reduced  $\beta$ -TG levels due to hypoproduction of platelet were found in contrast to elevated FPA levels. On the other hand, in the patients with gastric cancer complicated with DIC, FPA levels elevated very slightly possibly due to extremely low concentration of fibrinogen, and  $\beta$ -TG levels showed a significant elevation. These results suggest that the measurement of both FPA and  $\beta$ -TG lead us to precise and accurate comprehension of coagulation abnormality. In the patients with overcompensated DIC, elevated FPA and  $\beta$ -TG levels (mean FPA: 11.7, mean  $\beta$ -TG: 98.0 ng/ml) were found, indicating hypercoagulability. Additionally, we tried to use the ultrafiltration apparatus instead of dialysis tubing to shorten a time required for FPA assay, because dialysis tubing for plasma dialysis requires a lot of time, and is inappropriate for clinical investigation, especially in an emergency.