Tuesday, July 14, 1981

Oral Presentations

Fibrinolysis – IV

08:00–09:30 h

Serine Protease Inhibitors – I

09:45–11:00 h

Dominion Ballroom North

0248

08:00 h

A STUDY ON FIBRINOLYSIS INDUCED BY DEFIBRASE INFUSION.
M. Kato, M. Fujimaki and K. Fukutake. Department of Clinical Pathology, Tokyo Medical College, Tokyo, Japan.

When Defibrase as a defibrination agent was infused intravenously, it was followed by fibrinolytic phenomenon with release of FDP in high concentration. In this paper it will be reported which in actual inducer among fibrinopeptide A, des-A-fibrinmonomer and Defibrase itself in this occasion.

The activity of plasminogen tissue activator, plasminogen and γ_2 plasmin inhibitor were measured by chromogenic method using S-2322, S-2251 and S-2251 respectively and fibrinogen concentration was assayed by tyrosine method. FDP, plasminogen and α_1 plasmin inhibitor were also measured by immunological methods.

After the infusion of Defibrase into four normal adults fibrionlytic activities were detected on the plasminogen-free fibrin plate and followed by decrease of plasminogen and α_1 plasmin inhibitor and increase of FDP with plasminogen activator. On the other hand, Defibrase did not show any activities of plasminogen activator and plasmin. Therefore, it might be imagined that one of three substances including fibrinopeptide A, des-A-fibrinmonomer and Defibrase might be actual inducer of plasminogen activator from the vessel wall. When fibrinopeptide A separated from dog plasma was infused intravenously to dogs, no effect on fibrinolytic phenomenon, was indicated and, when the test-samples from the reflux experiments with Defibrase by the ues of dog's leg were applied on standard fibrin plate, weak fibrinolytic reaction were detected in a few cases. However, when des-A-fibrinmonomer was tested, increase of FDP, decrease of fibrinogen and α_1 plasmin inhibitor, showing the mode of dose-response, were detected in all cases of dog.

According to the results obtained above, it might be suggested that the actual inducer of fibrinolytic related with Defibrase infusion might be des-A-fibrinmonomer.

0249

08:15 h

PLASMINOGEN ACTIVATORS IN HUMAN MALIGNANT MELANOMA.
G. Markus, J. Madeja, J.L. Evers, G.H. Hobika, S.M. Camiolo, and J.L. Ambrus. Depts. of Experimental Biology and Pathophysiology, Roswell Park Memorial Inst., N.Y. State Dept. of Health, Buffalo, NY 14263.

The plasminogen activator (PA) content of metastatic malignant melanoma was determined in Triton X-100 extracts of 11 surgical specimens and adjacent normal tissue, using azocaseinolysis with added plasminogen. The mean PA content of the tumors was 8.4 ± 10 (SD) CTA u/g tissue (6 times that of the surrounding tissue), lower than found earlier in lung, colon and breast tumors. Inhibition by goat IgG against purified human urokinase showed that the predominant activator was of the UK type, as was the case with the tumors examined earlier, except those of the prostate. This is in contrast with recent reports which showed that human melanoma-derived cells secrete into the culture fluid almost exclusively the "vascular type" PA (Wilson et al., Cancer Res. 40, 933, 1980; Roblin and Young, Ibid. 40, 2706, 1980). While this type of PA was present in all extracts here examined, in 3 of them only trace amounts (<1%) could be found. The vascular type PA, when present, could be inhibited by rabbit IgG against human melanoma cell culture-derived vascular PA (kind gift of Dr. E. Dowdle). SDS-gel electrophoresis in conjunction with fibrin-agar overlay zymography showed multiple activator bands ranging in mol. wt. from 100,000 to 30,000. All but the 70,000 mol. wt. vascular type PA band were inhibited by inclusion of anti-UK IgG into the fibrin-agar mixture.

The discrepancy between the tumor extracts and the culture media may be due to a selective advantage of vascular type PA-secreting cells in culture, or to the turning off of the UK gene in the culture environment. It is also possible that production of vascular type PA is suppressed in vivo.

0250

08:30 h

A LIFE-LONG AND ULTIMATELY FATAL BLEEDING SYNDROME DUE TO GROSSLY INCREASED LEVELS OF PLASMA PLASMINOGEN ACTIVATOR.
B. Bennett, N.A. Booth, A.M. Cumming, I.A. Cook, A.A. Dawson, J. Knox. Department of Medicine, University of Aberdeen and Raigmore Hospital, Inverness, Scotland.

Episodes of haemorrhage due to increased fibrinolytic activity alone are uncommon and lifelong bleeding disorders due to excessive fibrinolysis are very rare. We report on a 46 year old male with a lifelong history of abnormal haemorrhage, usually occurring a day or two after minor trauma, surgery or dental extraction; no benefit had been derived from transfusion of fresh frozen plasma. There was no family history of bleeding but his father and grandfather had died at an early age of myocardial infarction and the patient had an abnormal lipid profile. No deficiency of any known clotting factor was present apart from a mild reduction of plasma fibrinogen (200mg/100ml). Platelet function was normal. The whole blood clot lysis time was consistently very rapid at 6-8 hours over a 2 year period of study. Levels of plasminogen, α_2-antiplasmin, α_1-antitrypsin, α_2-macroglobulin, antithrombin III and C_{1S} - inhibitor were normal but levels of plasminogen activator were grossly increased as were those of fibrin/fibrinogen related antigens (FRA).

He ultimately developed a massive spontaneous intracerebral haemorrhage which proved fatal after an illness lasting 7 days, during which administration of tranexamic acid abolished evidence of overactive fibrinolysis and resulted in a rapid rise of plasma fibrinogen to 700mg/100ml and a fall in FRA levels. Autopsy showed generalised severe atheroma. Thus the presence of grossly increased levels of fibrinolytic activity over many years did not prevent the development of atheroma in this patient in the presence of disordered lipoprotein metabolism though it may have contributed to the absence of thrombotic occlusions adjacent to atheromatous plaques.