MIXED POSTERS XII

Thrombosis

CLINICAL AND EXPERIMENTAL STUDIES ON THE BLEEDING TENDENCY DURING DEFIBRINOGENATION THERAPY.
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Defibrinogenation with thrombin-like enzyme is expected to be a new type of anticoagulant therapy without serious bleeding complications. However, it appears to be dangerous to perform surgical procedure in defibrinogenated state. In order to investigate the causes of the bleeding tendency which occurs during defibrinogenation therapy, the following clinical and experimental studies were undertaken. Ten mongrel dogs were used, the superior caval vein was replaced by expanded polytetrafluoroethylene graft. 50 to 100 μ l/kg of batroxobin was administered 2 days prior to the operation. 5 out of 10 dogs died due to bleeding postoperatively, and the causes of the bleeding seemed to be the decreased fibrinogen concentration and the reduced platelet function. Fifteen patients suffering from peripheral vascular thrombosis were treated with 30 to 60 μ l/kg of batroxobin. In 9 patients, urokinase was administered combined with batroxobin. No bleeding complications were observed in these patients. In another 6 patients, surgical procedure was performed after batroxobin administration. Postoperative bleeding was observed in one out of these 6 patients. This patient was operated on after the initial administration of batroxobin. FDP level was 512 μ g/ml and ADP induced platelet aggregation was within normal limits, but fibrinogen concentration was unmeasurable at the time of operation. The cause of the bleeding seemed to be the decreased fibrinogen concentration. From these clinical experiences, it is suggested that platelet adhesion to glass and ADP induced platelet aggregation are not influenced by the decreased fibrinogen concentration nor the increased level of FDP during the defibrinogenation therapy with batroxobin. These results indicate that an adequate level of fibrinogen is needed for certain hemostasis besides normal platelet function.

In vivo effects of human granulocyte neutral proteases on blood coagulation in green monkeys (*Cercopithecus aethiops*)

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Two neutral proteases (elastase-like = ELP, and chymotrypsin-like = CLP) derived from human PMN in highly purified form inactivate in vitro human isolated coagulation factors (Thromb. Res. 6, 315, 1975). These effects can be observed also in human plasma, despite its high antiprotease capacity. (Blood February 1977).

ELP and CLP (both free of endotoxin) were infused into green monkeys either separate or in combination to investigate a possible role of these proteolytic enzymes also in vivo. Activity of coagulation factors I - XIII and antiprotease potential has been followed for a 24 hour period in short intervals.

A loss of activity of coagulation factor II, V, VIII, IX, X and XIII could be demonstrated. Fibrinogen concentration decreased and fibrinogen split products could be detected. In two-dimensional immunoelectrophoresis α_1 -antitrypsin-ELP and α_2 -macroglobulin-ELP-complexes were demonstrable for about 6 hours after protease infusion. Bleeding complication occurred after injection of both enzymes.

The results indicate a direct proteolysis of coagulation factors by PMN neutral proteases in vivo.

We suggest that similar conditions are present in patients with acute leukemia or septicemia.