399

INFRACLINIC ACTIVATION OF PLATELETS AND FIBRIN FORMATION IN CANCER PATIENTS. J.L. David (1)(2), M. Lambrichts (2) and M.T.Closon (2). Thromb-Hemost. Unit.(1) Oncology Dep. (2) Univ. Liège, Belgium.

Thromboembolism has been frequently reported in cancer patients, mainly in cases with solid tumors. Besides in several animal models, fibrin deposition around the tumor and platelet aggregates appear to be involved in invasion and metastasis. This study was aimed at evaluating the extent of in vivo platelet activation and fibrin formation in several kinds of human cancer. We excluded from this study patients whose blood was sampled with difficulty as well as those having clinical evidence of thrombosis or embolism, those with thrombocytopenia, increased fibrinogen degradation products or biological pattern of disseminated intravascular coagulation. Fibrinopeptide A (fpA) and β-thromboglobulin (β-tg) were determined by RIA. Free platelet count ratio (PCR) was determined on whole blood samples as an index of circulating aggregates. Usual coagulation tests, antithrombin III activity, protein C plasma level, F VIII related antigen (F VIII RAG), F VIII Ristocetin cofactor (F VIII RCF) and F VIII procoagulant activity (F VIII C) were also determined.
It was found that in more than fifty percent of patients, fpA was significantly increased above the upper reference limit. Cases with increased B-tg were less frequent. Separate increases in β-tg or fpA levels were often observed. PCR remained within the reference values in almost all patients. F VIII RAG, RCF and C were usually above 150 % of the reference mean.
We conclude that platelet release and fibrinoformation frequently occur in cancer patients showing no sign of thrombotic process. Increased level of fpA with normal plasma β-tg level suggests that thrombin generation occurs only in the extravascular compartment, probably next to the tumoral tissues. Increased levels of plasma β-tg with normal fpA levels may result from platelet activation by other stimuli than thrombin. It must be emphasized that normal PCR does not exclude the presence of fibrinous circulating aggregates which cannot be dispersed by EDTA. High F VIII activities may be due to the release of the von Willebrand factor from tumoral vessels.

400

CHARACTERISATION OF PLATELET AGGREGATING MATERIAL EXTRACTED FROM HUMAN LUNG ADENOCARCINOMA CELL LINE WHICH METASTASIZED IN NUDE MICE S,C, IMPLANTATION. H. Inufusa, N. Sagara, K. Nakano and M. Yasutomi. Department of 1st Surgery, KINKI University School of Medicine, Minamikawachi-gun, OSAKA, JAPAN.

It has been reported in animal experimental system that Platelet Aggregating Material (PAM) of cancer cell play important role in cancer metastasis. Many human cancer cell lines has been also studied the platelet aggregation activity of PAM. But correlation between the platelet aggregation activity and metastatic potential of human cancer cells were usually unknown. We established a human lung adenocarcinoma cell line KUM-LK-2 which produce spontaneous lung metastasis when cells implanted into subcutaneous of nude mice. PAM was extracted from KUM-LK-2 cells following the method of D.Mohanty and P.Hilgard. Platelet aggregation study of PAM was performed by human Heparinized platelet rich plasma useing NIKO Hematracer PACT2D. Character of PAM were examined by physical and chemical treatment. KUM-LK-2 PAM show 80% of platelet aggregation in maximum after 150 sec lag time, and aggregation was not found by Citrated PRP.

Treatment			Aggregation (%Max)	Lag time (Sec)
Heat treat	56°C 30min		-	-
Freeze and thaw	3-5 times		80	150
Supernatant of centrifugation	100,000 Xg, 1h		-	-
Addition				
EDTA	3.8mM	of PRP	80	150
Indomethacin	0.05mM	of PAM	80	150
Neuraminidase	8U/ml	of PAM	80	150
Plasmin	10U/ml	of PAM	40	240
Phospholipase C	92u/ml	of PAM	-	-
DOG	0.8µ/ml	of PRP	-	-

It is concluded that PAM is high moleculer protein and contain Phospholipid and aggregation activity is concerning with ATP composition of platelet. PAM dose not contain Fibrinogen and Sialic acid, and not concern with Thromboxan composition. This study is first case of platelet aggregation activity of PAM extracted human cancer cells which contain metastatic potential.

401

PLATELET ACTIVATION BY HUMAN CANCER CELLS GROWN "IN VITRO" OR DISSOCIATED FROM TUMOUR TISSUES.
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The mechanisms of platelet activation by human tumour cells grown "in vitro" or freshly dissociated from tumour tissues have been investigated.
MoCCL human T-lymphoblastic cells cultured "in vitro" induced platelet aggregation through the production of ADP, as evidenced by inhibition of the effect by apyrase. The maximum of ADP production by tumour cells was reached after 1 hour and was 225 p moles/10^6 cells.
On the contrary, platelet aggregation induced by 5637 human bladder carcinoma cells was not inhibited by apyrase, but was abolished by hirudin, indicating the important role of thrombin in this effect.
Tumour cells dissociated from 3 breast carcinomas showed a very high platelet aggregating activity, which was not inhibited by hirudin or apyrase, but was abolished by iodoacetic acid, suggesting a role for a cystein-protease in platelet activation.
These results confirm that platelets can be activated by tumour cells through different mechanisms; they also suggest that the methods employed to obtain the tumour cells can influence the results, probably because of the different cell populations which are present in the dissociated tumour tissues.
Informations obtained with freshly dissociated cells are interesting, because this method has been used seldom so far and because it provides a more physiological approach to the study of the interactions of tumours and platelets.

402

PLATELET MEMBRANE GLYCOPROTEINS ABNORMALITIES IN PATIENTS WITH ACUTE LEUKEMIAS AND MALIGNANT LYMPHOMAS.
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Membrane glycoproteins are implicated in platelet functions.In myeloproliferative disorders some of the platelet functions are known to be perturbated and an abnormal glycoproteins pattern was demonstrated earlier.In this study flow cytometry analysis of human platelet membrane glycoproteins IIa and IIIa in patients with acute leukemias and malignant lymphomas has been performed using monoclonal antibodies against these glycoproteins.

group examined	% of all platelets labelled mean±SD		% of platelets labelled in the region of fluorecsence mean ± SD			
			low density		high density	
	GP IIa	GP IIIa	GP IIa	GP IIIa	GP IIa	GPIIIa
donors	82±12	77±13	26±12	23±14	48±20	51±10
ALL	64±12	64±9	42±18	51±21	34±12	33±17
AML	63±6	64±7	53±14	50±17	33±7	35±10
NHL	66±12	67±13	39±15	40±14	47±10	42±10

A reduction in number of glycoproteins receptors on platelet membrane was demonstrated in patients with acute leukemias and malignant lymphomas in comparison with platelets of healthy donors.In patients with leukemias the positive correlation of percentage of platelets recovered in various density receptor regions to bleeding time and negative correlation to platelet number for both glycoproteins have been found.The study demonstrated that flow cytometry can be a useful method of analysis of platelet membrane glycoproteins,and that the patients with acute leukemias and malignant lymphomas have the number of glycoproteins reduced.