MIXED POSTERS X

Platelets

CYCLIC NUCLEOTIDE PHOSPHODIESTERASE IN PLATELETS AND PLATELET AGGREGABILITY. H. Yamazaki, T. Motomiya, N. Mashimo, T. Asano and H. Hidaka. The Tokyo Metropolitan Institute of Medical Science, Tokyo, Aichi Prefecture Colony, Kasugai and Kyoto University, Kyoto, Japan.

Though roles of cAMP and cGMP in platelets are thought to be important on platelet aggregation, little information on their phosphodiesterase (PDE) is available. Platelet interaction with various vessel walls might be reflected on cyclic nucleotides and their PDEs. cAMPPDE and cGMPPDE in platelets and platelet aggregability were measured in 22 healthy volunteers (41.0±14.2 yrs, mean±SD), 26 arteriosclerotic patients (58.4±8.7 yrs) and other miscellaneous patients excluding vascular diseases (44.9±16.4 yrs). PDE activities were measured by the Hidaka and Shibuya method (Biochem. Med., 10:301, 1974). Platelet aggregation induced by ADP and epinephrine was recorded by Sienco aggregometer. Activities of cAMPPDE and cGMPPDE of platelets were 2.37±0.52, 7.23±1.87 in the healthy, 2.50±0.85, 7.53±2.60 in the arteriosclerotics and 2.38±1.02, 6.98±2.59 pmol/min/10^7 platelets in the miscellaneouus patients respectively. No significant difference was observed among the three groups. Platelet aggregabilities also showed no significant difference. However there was a significant inverse correlation between the aggregability by 1 ug/ml of epinephrine and the PDE activities only in the arteriosclerotic patients. The correlation coefficients were -0.61 between the primary aggregation and cAMPPDE, -0.65 between the primary aggregation and cGMPPDE, -0.58 between the 5 min aggregation and cAMPPDE and -0.76 between the 5 min aggregation and cGMPPDE. The slopes in regression lines of cGMPPDE were far steeper than those of cAMPPDE. Aggregability and cyclic nucleotide metabolism in circulating platelets may be affected by arteriosclerotic vessel walls.

PLATELET DYSFUNCTION WITH GLUTATHIONE REDUCTASE DEFICIENCY AFTER 1,3-BIS(2 CHLOROETHYL)-1-NITROSOUREA. R. McKenna, T. Ahmad, H. Frischer. Rush Presbyterian-St. Luke's Medical Center - Rush University, Chicago, Illinois, USA.

We have previously shown that patients receiving antitumor chemotherapy with 1,3-bis-(2 chloroethyl)-1-nitrosourea (BCNU) rapidly acquire a severe generalized glutathione reductase (GSSG-R) deficiency. We now report that when platelets were exposed in vitro to BCNU (30 minutes, 37°, at 10^{-3} M, six separate studies), the resulting GSSG-R deficiency was associated with marked impairment of platelet aggregation in response to ADP (1 µM and 3 µM), to epinephrine and to collagen (all p's < 0.001). Platelet factor 3 availability was also markedly reduced ($p < 0.001$); prothrombin consumption and glass adhesiveness were unaffected. In additional experiments to evaluate the dose response relationship, epinephrine induced aggregation was abnormal at 5×10^{-6} M BCNU, ADP (1 µM) induced aggregation was abnormal at 10^{-5} M BCNU, while ADP (3 µM) and collagen aggregation became abnormal at 5×10^{-5} M BCNU. GSSG-R deficiency (less than 11% of control activity), without glucose-6-phosphate dehydrogenase and 6-phosphogluconic dehydrogenase deficiencies, preceded all platelet abnormalities. We have demonstrated that a specific platelet GSSG-R deficiency after BCNU precedes the development of severe platelet dysfunction.