Time

15.15 0608 IMMUNE INJURY TO HUMAN PLATELETS MEDIATED BY IgG Fc RECEPTOR IS PREVENTED BY PROSTACYCLIN

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Immune injury to human platelets by drugs, bacteria, and viruses which form antigen-antibody complexes is mediated by the IgG Fc receptor on human platelets and results in thrombocytopenia. We studied whether immune injury to human platelets mediated by the IgG Fc receptor can be prevented by prostacyclin (Prostaglandin I_2, PGI_2), a novel prostaglandin generated by the blood vessel wall. Immune injury to human platelets in whole plasma was elicited by Protein A-bearing staphylococci. Protein A induces binding of I to the human platelet Fc receptor, which results in platelet aggregation and ^{3}H-serotonin release in whole plasma. Excess of isolated Fc fragment inhibits aggregation and serotonin release in this model of immune injury. Synthetic PGI_2 protected human platelets from this IgG Fc fragment-mediated immune injury in whole plasma. Inhibition was prompt (1 to 5 min) and dose dependent, reaching maximum at 10^{-6}M of PGI_2. Removal of plasma proteins and use of IgG-coated cells did not change the inhibitory potency of PGI_2, which was at least 1000-fold more active than 6-keto $PGF_{1\alpha}$. Electron microscopy revealed that PGI_2 prevented binding of IgG-coated cells to human platelet membrane. From comparison with anti-inflammatory steroids (methylprednisolone) and nonsteroidal prostaglandin synthetase inhibitors (ASA), it appears that prostacyclin is the most active agent known to date to protect human platelets from IgG Fc receptor-mediated immune injury in vitro.

15.30 0609 POST-TRANSFUSION PURPURA (PTP) - A MULTIFACETED ENIGMA

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A 61 yr. old woman presented with thrombocytopenia and diffuse bleeding which developed days after a colon resection and transfusion of 6 units of blood. Her serum contained an IgG antibody (AB) which aggregated platelets from 60% of normal donors. Using the ^{51}Cr release technique and indirect immunofluorescence, strongly positive reactions were seen at a serum dilution of 1:100 with 50% of platelets from a panel and with 90% at a 1:250 dilution. Strongly positive reactions were seen with 96% of cells from a lymphocyte panel. Unlike classical PTP, her serum reacted strongly with platelets from 3 of 5 $P1^{A1}$ negative donors. In 3 donors, platelets, which failed to aggregate with pt. serum, aggregated with serum known to contain AB to $P1^{A1}$ platelets. Inhibition of platelet aggregation (PA) resulted when anti-IgG was incubated with pt. serum. Prostacyclin, (PGI_2), 0.025 to 1 µM, also inhibited PA by pt. serum. A cytotoxic AB, requiring complement, was demonstrated against cultured human endothelial cells using fluorescence microscopy with the vital dye diacetyl fluorescein and ethidium bromide. Thus, PTP may involve platelet antigens other than $P1^{A1}$, and multiple antibodies may operate in its pathogenesis. Of particular importance was the demonstration of an AB against endothelium which may have been involved in the production of early, lethal hemorrhage.

15.45 0610 PLASMA BETATHROMBOGLOBULIN MEASUREMENT TO DIFFERENTIATE TYPES OF THROMBOCYTOPENIA

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It is important to differentiate between extravascular (autoimmune thrombocytopenia, ATP) and intravascular (thrombotic thrombocytopenia, TTP) platelet destruction in thrombocytopenia. Betathromboglobulin (BTG), a platelet-specific protein with a plasma half life of 20 minutes is released in-vivo from platelets by various stimuli and may reflect platelet activation or destruction. BTG concentration can be measured in plasma using a radioimmunoassay to a sensitivity of 1 ng/ml., (normal 28.0 ± 8.0 ng/ml., n = 70). Plasma BTG was measured in 3 patients with ATP (platelet counts: 17, 20, 16 x 10^9/L) and 2 patients with TTP (platelet counts: 20, 40 x 10^9/L). In ATP, BTG was normal (22, 11, 17 ng/ml.) and in TTP, BTG was elevated (80, 72 ng/ml.). Plasma BTG remained normal in ATP after treatment. BTG remained elevated in TTP (120 ng/ml.) even when the platelet count became normal (220 x 10^9/L) but while fragmented RBC were still present and became normal (21 ng/ml.) on complete recovery. These data suggest that plasma BTG may be useful in differentiating extravascular from intravascular platelet destruction by detecting increased concentrations of BTG in plasma.