PLATELET ACTIVATING FACTOR (PAF) is generally considered to play an important role in acute allergic reactions. A special example of such a reaction is allergic asthma and indirect evidence suggests that here too PAF may be involved. Direct proof for a role of PAF, however, is difficult to obtain since in blood PAF has an extremely short half-life due to its inactivation by an acetyl-hydrolase in plasma, its uptake and degradation by many cell types and its lipophilic properties making it easily stick to membranes. Despite these handicaps we report here that during an acute bronchoconstrictive reaction in asthmatics, PAF is liberated into the circulation and binds to platelets. Eight patients with allergic asthma were challenged by inhalation provocation. Four patients responded with an immediate bronchoconstrictive reaction, which was accompanied by a 40% decrease in freely accessible PAF-receptors on their platelets, collected 1 hour after bronchoconstriction (specific bindings of 3H-PAF decreased from 264 ± 44 to 164 ± 45 pmol/platelet, p < 0.05). The patients who did not respond to allergen provocation failed to show a change in 3H-PAF binding. In both groups platelet counts and PAF-induced aggregation did not change significantly. In view of the high specificity of PAF-receptors on platelets (a 200-fold excess of histamine did not interfere) and the fact that in vitro their binding gradually becomes irreversible, we conclude that during an immediate bronchoconstrictive reaction circulating platelets make contact with PAF. Together with evide nce that under similar conditions secreted products from platelets appear in the circulation, these data indicate that platelet activation by PAF forms an important step in the pathophysiology of allergic asthma.

HUMAN PLASMA PAF-ACETYHYDROLASE, NORMALLY PRESENT IN LOW DENSITY LIPOPROTEINS, IS ASSOCIATED WITH HIGH DENSITY LIPOPROTEINS IN A PATIENT WITH LDL DEFICIENCY. L. Surve, J.W.N. Akkerman, Dept. of Haematology, University Hospital, P.O.Box 16250, 3500 CG Utrecht, The Netherlands.

Platelet Activating Factor (1-O-alkyl-2-acetyl-sn-glycerol-3-phosphocholine; PAF) plays an important role in acute allergic and inflammatory reactions and activates platelets in the nanomolar range. One of the main factors that controls PAF activity in blood is an enzyme, acetylhydrolase, which converts PAF to biologically inactive lyso-PAF. The enzyme is acid labile and normally associated with apo B-containing low density lipoproteins (LDL, density 1.006-1.063 g/ml), which are typical for HDL.

We investigated whether a deficiency in LDL would affect the enzyme activity. PAF-inactivating activity was measured in plasma from a patient with abetalipoproteinemia, a rare autosomal recessive disorder, characterized by the absence of apo B and apo B-containing lipoproteins (chylomicrons, VLDL and LDL). Plasma triglyceride was 0.2 mmol/l (normal 1.40-2.20 mmol/l) and cholesterol 1.3 mmol/l (normal 5.0-7.70 mmol/l). Separation of lipoproteins by density gradient centrifugation revealed a slightly decreased HDL content whereas VLDL and LDL were below the detection limit (0.20 mmol/l: based on cholesterol content).

Despite the absence of LDL, PAF-inactivating activity was measurable in plasma of the patient (measured by (i) the decrease in aggregation inducing activity of PAF after incubation, (ii) the conversion of 1H-PAF to lyso PAF, separated on TLC, (iii) the liberation of 3H-tartrate from 3H-PAF was present and even slightly higher than in normal plasma (hydrolysis of 3H-PAF after 20 minutes incubation was 78 ± 42 and 65 ± 62% in patient and controls, respectively). Subfractionation revealed that the enzyme activity was present in fractions with densities of 1.063-1.214 g/ml, which are typical for HDL.

These results indicate that PAF-acetylhydrolase, although normally present in LDL, binds to HDL in a patient with extreme LDL-deficiency.

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The first steps of the de novo synthesis of alkoxyacyl lipids, like plasmalogens and platelet activating factor (PAF) are localized in the peroxisome. We have previously reported the severely impaired PAF synthesis in Zellweger patients. These patients lack cytochemically detectable peroxisomes, and have a severely impaired alkoxyacyl lipid synthesis. However, chondro dysplasia punctata (CDP) patients have also been shown to have an impaired alkoxyacyl lipid synthesis. We therefore investigated PAF synthesis in CDP patients.

Platelets and leucocytes were isolated from 3 CDP patients Leucocytes from normal controls produced 4678 ± 2033 pmoles PAF/10^6 cells (n=6, range 1698-7058) when optimally stimulated with Ca^{2+}, ionophore A23187. Normal control platelets produced 0.6 ± 0.3 pmoles PAF/10^6 cells (n=6, range 0.2-1.0) when optimally stimulated with thrombin. PAF synthesis by the leucocytes of the patients was severely reduced, but detectable. Leucocytes from patient 1, 2 and 3 synthesized 9.660 and 325 pmoles PAF/10^6 cells respectively. Platelets from the patients 1, 2 and 3 synthesized 0.1, 0.2 and 0.2 pmoles PAF/10^6 cells respectively.

Platelet aggregation, induced by ADP, PAF or thrombin (also in the presence of inhibitors of the first and second pathway of platelet activation) was normal.

We conclude that PAF synthesis is severely impaired in leucocytes and platelets from CDP patients. The residual platelet PAF-synthesis may suffice to warrant normal platelet functioning.

INTERACTIONS BETWEEN PLATELETS AND NEUTROPHILS HAVE BEEN REPORTED FOR THE PRODUCTION OF SEVERAL MEDiators OF INFLAMMATION SUCH AS HYDROGEN PEROXIDES OR LEUKOTRIENES. ANOTHER POTENTIAL MEDiator OF THROMBOSIS AND INFLAMMATION IS PAF-ACETHER WHICH IS SYNTHESIZED BY ACTIVATED PLATELETS AND NEUTROPHILS. SINCE PLATELETS FORM AND RELEASE LARGE AMOUNTS OF THE PAF-PRECURSOR LYSO-PAF, PLATELETS AND NEUTROPHILS COOPERATE FOR THE FORMATION OF PA f-ACETHER (PLATELET-ACTIVATING FACTOR).

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