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Platelet Dysfunction in Splenectomized Patients with Hairy Cell Leukemia

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Abstract—*Platelet function was assessed in 17 patients with hairy cell leukemia who had undergone splenectomy. Defective PAF-induced aggregation and selective reduction of β-thromboglobulin were found in platelets from six and eight patients respectively. These defects were not necessarily associated with bleeding complications.*

INTRODUCTION

HAIRY cell leukemia (HCL) is a distinct clinico-pathological entity, in which, after infection, hemorrhage is the second most frequent cause of death [1]. Apart from thrombocytopenia, it has been reported that platelets may be qualitatively defective in HCL. The precise mechanism by which platelets are altered is however not clear but hairy cells (HC) might interact with platelets to induce a release reaction [2]. Platelet function in patients with HCL who have undergone splenectomy has not been extensively investigated. We therefore assessed several parameters of platelet function in 17 consecutive, unselected HCL patients who had undergone splenectomy and had slightly reduced or normal platelet count.

CLINICAL AND LABORATORY DATA

Thirteen males and four females (aged 35–76 yr) were studied. Twenty males and 11 females (aged 30–60 yr) acted as controls. All patients fulfilled the clinical and hematological criteria of HCL [3] and had undergone splenectomy at least 1 month before the study because of persistent pancytopenia. Before splenectomy platelet count was low (50–100 platelets × 10^9/l), but at the time of this study it ranged from 150 to 450 × 10^9/l except in three patients who were thrombocytopenic: 90–98–110 platelets × 10^9/l. Bleeding time measured in duplicate using a disposable device (Simplate II, General Diagnostics, NJ, U.S.A.) was normal in all but one HCL patient (> 15 min), while a bleeding tendency was found in three cases. Platelet aggregation studies were done as previously described [4]. Arachidonic acid (AA) (99% pure — Sigma, St Louis, MO) was prepared as sodium salt and kept under nitrogen as described [5]. Pure synthetic 1-0-octadecyl-2-acetyl-sn-glycero-3-phosphorycholine (PAF) was obtained from Bachem Feinchemikalien, Budendorf (Switzerland). Platelet aggregation abnormalities were found in six out of 15 patients studied (40%).

In all six cases, only one reversible wave of aggregation was induced by PAF (up to 400 nM). In one patient this defect was isolated, in another one it was accompanied by reduced response to collagen and in the other two by reversible ADP-induced aggregation. Defective aggregation by all stimuli was observed in the remaining two patients (one had prolonged bleeding time). In all six patients the defective response to PAF was normalized after pre-exposure to subthreshold concentrations of adrenaline (Fig. 1). Platelet serontonin (5HT) content in 15 patients [6] was not significantly different (0.28 ± 0.10 nmol/10^8 platelets) from 27 controls (0.29 ± 0.07 nmol/10^8 platelets). β-thromboglobulin was measured in platelet-poor plasma (Pl-beta TG) and in platelets (Plt-beta TG) lysed with Triton x-100 [7], using a commercial kit (Radiochemical Centre, Amersham, U.K.). β-TG ratio was determined according to Zahavi *et al.* [8]. Eight out of 15 patients had platelets with a low β-thromboglobulin content and three also had higher plasma β-thromboglobulin ratios than controls (Fig. 2). Thromboxane B2 (TxB_2) was measured by a radioimmunoassay using a commercially available kit (New England Nuclear, Boston, MA). Generation of platelet TxB_2 induced by endogenous

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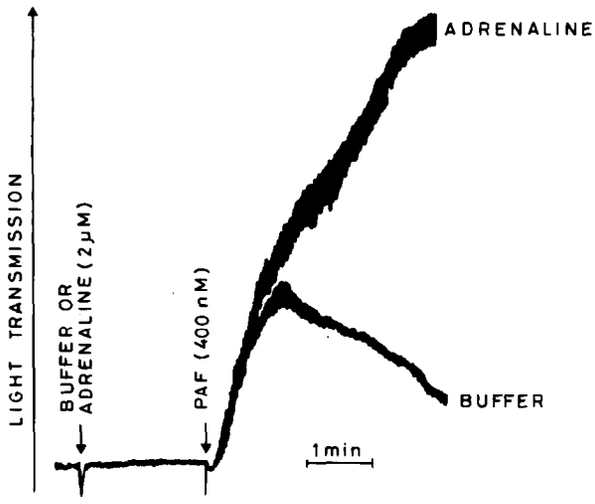

Fig. 1. Representative platelet aggregation tracings by PAF after exposure of platelets to subthreshold concentrations of epinephrine.

thrombin, ranged between 45 and 209 ng/ml in controls and was markedly reduced (4.6–33 ng/ml) in serum from five patients. After platelet challenge with A.A. (0.5–1 mM) in four cases (those with reduced serum TxB_2) platelets generated less TxB_2 than the controls at all AA concentrations.

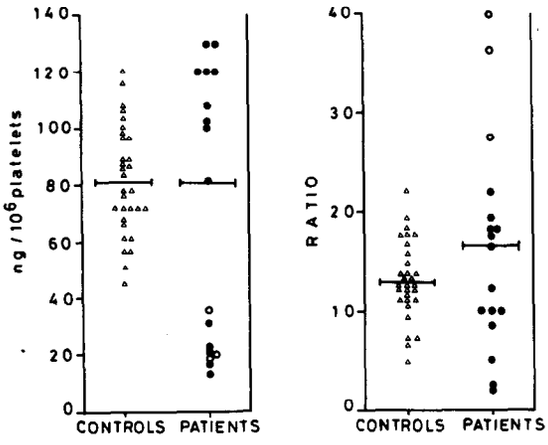

Fig. 2. Platelet β-thromboglobulin (left panel) and plasma β-thromboglobulin ratio (right panel) in controls (C) and HCL patients (P). Open circles (○) indicate cases with low platelet β-thromboglobulin values and high plasma β-thromboglobulin ratios.

DISCUSSION

Only three out of 17 patients with HCL who had undergone splenectomy presented with a bleeding tendency and only one had prolonged bleeding time and recurrent hemorrhagic symptoms. However, *in vitro* platelet dysfunction was found in six out of 15 cases.

Qualitative platelet disorders had also been reported by previous studies in patients with HCL [2,9,10]. An original observation was that adrenaline made irreversible the defective PAF-induced aggregation, observed in six patients. HCL platelets might have a defective amplification mechanism of the primary response to PAF, an anomaly similar to that recently found in patients with chronic myeloproliferative disorders [11].

The possibility of a storage pool or release defect prompted further investigation on platelet granules content and arachidonic acid metabolism.

Serotonin content of platelet dense granules was not significantly reduced in HCL patients, but more than half of the patients had a low content of alpha-granule located β-TG. A similar pattern was found by Harker *et al.* [12], in patients undergoing cardiopulmonary by-pass.

Arachidonic acid metabolism was also moderately impaired in platelets from HCL patients. In 1/3 of cases TxB_2 release induced by both endogenous thrombin and exogenous AA was reduced.

It was not the purpose of this study to compare platelet function in HCL patients before and after splenectomy. Thus we cannot prove or disprove that splenectomy corrects platelet dysfunction or bleeding time in these patients. It can safely be concluded, however, that platelet function was defective in several patients with HCL who had undergone splenectomy. The defect was heterogenous.

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