

LETTER

Platelet Aggregation, Platelet Serotonin and Pancreatitis

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Dear Sir:

The article by Mimidis *et al.* [1] prompted us to contribute some additional information. The authors studied acute pancreatitis patients showing increased platelet adhesiveness and aggregation. They postulate that the platelet activation factor is the most important mediator involved in the process and triggers platelet activation. They also discuss the mechanisms played by the membrane integrin glycoprotein IIb/IIIa. Furthermore, they made reference to membrane receptors for fibrinogen and the calcium-dependent linkage formation between activated receptors and bivalent fibrinogen which results in platelet aggregation. They also referred to pro-aggregatory mediators such as ADP, ATP, platelet factor 4 (PF4), betathromboglobulin (beta-TG), thromboxane A₂ (TXA₂), fibrinogen and thrombospondin which are followed by the translocation of alpha-granule membrane protein P-selectin (CD62). Finally, they mentioned the role played by phosphatidylserine which is the starting point for the coagulation cascade. They also referred to the alterations of the platelet function described in models of systemic inflammation such as ulcerative colitis, Crohn's disease and acute pancreatitis. With respect to all of the above, we would like to further elucidate the role played by platelet-serotonin (p-5HT) in thrombogenesis. This factor, rather than the platelet count, seems to constitute the true index of thrombogenesis [2, 3]. With respect to the

above, we successfully treated five cases of refractory idiopathic thrombocytopenic purpura (ITP) using a neuropharmacological therapy aimed at enhancing (central nervous system) noradrenergic activity. Surprisingly, restoration of p-5HT levels, rather than the platelet count, was correlated with bleeding stoppage and clinical improvement. The above findings are consistent with the fact that serotonin is stored in the delta granules of platelets.

The release of serotonin is considered to be the "gold standard" assay for the detection of thrombocyte activation [4]. The presence of serotonin is covalently linked to fibrinogen bound on the surface of the activated platelet where it increases the retention of procoagulant factors on the cell surface [5]. Serotonin, therefore, occupies a central role in the hamostatic process, and its release is considered the most reliable assay for platelet activation [4].

Our findings are in line with those obtained by Dominguez *et al.* [6] who showed a lack of correlation between the platelet count and bleeding in an experimental model of immune thrombocytopenic purpura in mice. The fact that not only acute pancreatitis [7, 8] but other inflammatory diseases, such as ulcerative colitis [9, 10] and Crohn's disease [11, 12, 13], showed similar platelet disorders is consistent with findings which show that these diseases present with increased platelet aggregability secondary to the elevated circulating adrenaline which is always present. The latter phenomenon is responsible

both for the reduction of p-5HT and the increase of plasma serotonin (f-5HT). Thus, we believe that the fundamental role played by platelet serotonin in thrombogenesis should not have been omitted in the discussion of the article by Mimidis *et al.* [1].

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Keywords Pancreatitis; Platelet Adhesiveness; Platelet Aggregation; Serotonin; Thrombosis

Abbreviations beta-TG: betathromboglobulin; f-5HT: plasma serotonin; ITP: idiopathic thrombocytopenic purpura; PF4: platelet factor 4; p-5HT: platelet-serotonin

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REPLY

Dear Sir:

In response to the letter of Drs. Lechin and van der Dijs [1], we would like to express our

gratitude concerning the additional information presented by the author. Indeed, the crucial role of platelet-serotonin (p-5HT) has been well-established in thrombogenesis and the release of serotonin has been proposed as the “gold standard” assay for the detection of thrombocyte activation [2].

However, the purpose of our study was to test a newly developed method of evaluating primary hemostasis based on the platelet function analyzer (PFA-100TM) in a prethrombotic model such as acute pancreatitis. This method had only been applied to hemorrhagic diathesis and its usefulness in thrombosis was unknown [3, 4, 5, 6]. Thus, we focused on testing the specific method rather than commenting on the underlying pathophysiology of platelets in acute pancreatitis.

In conclusion, the authors’ statements regarding the p-5HT levels and the potent use of selective serotonin-reuptake inhibitors (SSRIs) in acute pancreatitis serve as a valuable proposal for future studies.

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Keywords Platelet Adhesiveness; Platelet Aggregation

Abbreviations p-5HT: platelet-serotonin; SSRIs: selective serotonin-reuptake inhibitors

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