

Piastrine: Alterazioni qualitative o quantitative

DIAGNOSTIC VALUE OF PLATELET GRANULE CONTENT AND RELEASE IN PATIENTS WITH INHERITED PLATELET FUNCTION DISORDERS WITH NORMAL PLATELET AGGREGATION

L. Bury, E. Petito, E. Falcinelli, V. Fazzi, A.M. Mezzasoma, P. Gresele

Department of Medicine and Surgery, Section of Internal and Cardiovascular Medicine, University of Perugia, Italy

Background and Aims. Inherited platelet function disorders (IPFD) are a heterogeneous group of rare bleeding disorders characterized by dysfunctional platelets. Establishing a definitive diagnosis of IPFD is crucial not only for providing personalized treatment and accurate prognostic assessment, but also for genetic counseling and family screening. This is particularly important for IPFDs associated with a high risk of bleeding and linked to potentially severe syndromic manifestations. However, the diagnosis of IPFD is complex and requires first-, second-, and third-level laboratory tests. The “gold standard” test for the diagnosis of IPFD is light transmission aggregometry. However, this method may lack sensitivity in detecting platelet α- and/or δ-granules content and/or release defects, thereby limiting their identification. The ISTH guidelines for IPFD diagnosis recommend the evaluation of platelet granule release and content as a first- and second-line tests, respectively (PMID: 25403439). However, an international survey showed that fewer than 50% of specialized laboratories assess platelet granule content and/or release tests during the diagnostic work-flow of a suspected IPFD, and, when they do it only as a second-line test (PMID: 24976115). Our aim was to explore the diagnostic value of assessing platelet α- and δ-granules content and/or release as first-line laboratory investigations in patients with IPFD but normal platelet aggregation.

Methods. We enrolled 39 patients with 11 different forms of IPFD diagnosed according to strict laboratory criteria and we performed the following first- and second-level diagnostic tests: light transmission aggregometry, platelet α-granule content and release (P-selectin expression by flow cytometry, and β-thromboglobulin content and release by ELISA), platelet δ-granule content and release (mepacrine uptake and release by flow cytometry, and ATP content and release by lumi-aggregometry)

Results. 26% of the enrolled patients (10 over 39), despite having a diagnosis of IPFD, exhibited normal platelet aggregation, and in particular: 5 patients with primary secretion defect, 2 with α/δ-granule defect, 2 with Hermansky Pudlak syndrome, 1 with familial platelet disorder predisposing to myeloid malignancies. Of the patients with normal platelet aggregation 40% showed defective α -granule content and 70% defective release. Moreover, 40% showed defective δ -granule content and 70% defective release. Overall, 70% showed defective content of α- or δ-granules and 100% defective release. Therefore, 100% of patients with normal platelet aggregation had a defect of α- or δ-granules. Measurement of β-thromboglobulin release detected more defects than assessment of P-selectin expression (70% vs 35% of patients). Results were comparable for assessment of mepacrine and ATP content and release (content: 40% vs 44%; release: 80% vs 70%).

Conclusions. Relying exclusively on light transmission aggregometry for the identification of IPFD may lead to overlooking the diagnosis of a non-negligible proportion of patients who can instead be identified through laboratory assays evaluating platelet α- or δ-granules release. The assessment of platelet granules should therefore be systematically included as first-line diagnostic test for suspected IPFD. Moreover, a test different from P-selectin expression may be advisable as alternative or additional test for the detection of α-granule defects.

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