The Official Journal of the Italian Society for the Study of Hemostasis and Thrombosis
SISET
Società Italiana per lo Studio dell'Emostasi e della Trombosi
Corso Nazionale SISET
Bergamo | 23-25 ottobre 2025

29TH NATIONAL CONFERENCE OF THE ITALIAN SOCIETY FOR THE STUDY OF HEMOSTASIS AND THROMBOSIS, 2025

ABSTRACT N. PO03

ENLARGED PLATELETS WITH REDUCED GP IB/IX CAN INDICATE DISORDERS OTHER THAN BERNARD-SOULIER SYNDROME.

C. Zaninetti[1], A. Marín-Quílez[2], S. Semenowitsch[1], A. Sánchez-Fuentes[2], A. Zamora- Cánovas[2], P. Gómez-González[2], E. Birgitte Leinøe[3], N. Fernández-Mosteirin[4], T. Murciano[5|6], C. Freyer[1], T. Thiele[1], J. Rivera[2|7], A. Greinacher[1].

1 Universitätsmedizin Greifswald, Institut Für Transfusionsmedizin, Greifswald, Germany, 2 Universidad De Murcia, Servicio De Hematología, Hospital Universitario Morales Meseguer, Centro Regional De Hemodonacion, Imib-Pascual Parrilla, Ciberer-U765, Murcia, Spain, 3 Rigshospitalet University Hospital, Dept. Of Haematology And Dept. Of Genomic Medicine, Copenhagen, Denmark, 4 Hospital Universitario Miguel Servet, Servicio De Hematología, Zaragoza, Spain, 5 Hospital Universitario Vall D'hebron, Servicio De Oncología Y Hematología Pediatricas, 6 Vall D'hebron Institut De Recerca, Barcelona, Spain, 7 Grupo Español De Alteraciones Plaquetarias Congénitas, Murcia, Spain. .

Background and aims:
Evaluation of platelet morphology is a cornerstone of the diagnostic work-up of patients with suspected inherited platelet disorders (IPD). We have established an immunofluorescence microscopy-based method on the peripheral blood smear in combination with light-microscopy as a screening--tool for IPD. The technique has been validated for 9 disorders displaying typical changes of platelet structure. As a quality-control of this approach, we regularly perform a blinded investigation of subjects, who had previously undergone genetic testing.

Methods:
Blood smears were stained using 13 primary antibodies against different platelet structures (alpha and dense granule, surface glycoproteins, cytoskeletal components) and 2 fluorescence-labelled secondary antibodies. Exclusively based on the morphologic evaluation, we formulated a possible diagnosis. After uncovering patients' information, we compared the anticipated defect with molecular outcome.

Results:
Over the last 12 months, we enrolled to this study 30 subjects. Based on the finding of platelet macrocytosis and reduced expression of the surface platelet glycoprotein (GP) Ib/IX, we predicted a diagnosis of Bernard Soulier syndrome (BSS) in 4 individuals. After unblinding molecular results, we could confirm the suspicion only in one case, in whom a pathogenic heterozygous deletion in GP1BB gene (c.236_244del [p.Pro79_Leu81del]) consistent with dominant-inherited BSS was found. In two subjects belonging to the same pedigree, a novel homozygous variant in the gene encoding for UDP-N-acetylglucosamine 2-epimerase (GNE): c.1516G>A [p.Gly506Ser] was found. In one individual, we found two novel variants in compound heterozygosis in the gene encoding for uridine diphosphate (UDP)-galactose-4-epimerase (GALE): c.382G>A [p.Val128Met] and c.590T>C [p.Ile197Thr]. All the three patients suffered from severe thrombocytopenia. In the patient with GALE mutations, a syndromic picture including mental retardation, mitral valve prolapse and hip malformation was also apparent.
Conclusion:
Platelet macrocytosis with reduced expression of GPIb/IX can indicate inherited thrombocytopenias due mutations in GALE or GNE. These two genes play a role at different levels of platelet production and clearance. In both disorders, the reduced externalization of GPIb/IX is a consequence of impaired protein glycosylation. Immunofluorescence microscopy on the peripheral blood smear and genetic testing complement each other.

Email: *carlo.zaninetti@uni-greifswald.de*