ReDIP, the Italian network for the diagnosis of congenital platelet function disorders

Dear Editor,

Congenital platelet function disorders (cPFD) are associated with an increased risk of mucocutaneous bleeding of various levels of severity; they may be classified based on abnormalities of platelet components that share common characteristics:[1] i) platelet receptors for adhesive proteins; ii) platelet receptors for soluble agonists; iii) platelet granules; iv) signal transduction pathways; v) procoagulant phospholipids; less well characterized PFD are grouped in a sixth category of miscellaneous abnormalities.[1] Although the prevalence of every single disorder is low, it has been shown that the overall frequency of cPFD might exceed that of von Willebrand Disease (VWD),[2] which was historically considered the most frequent congenital abnormality of hemostasis.[3]

The diagnosis of cPFD is complex because it requires the performance of specific tests that are not generally available in routine laboratories and require the involvement of expert and dedicated personnel in specialized centers. Careful assessment of the bleeding history is extremely important and could be done using the International Society of Thrombosis and Haemostasis Bleeding Assessment Tool score,[4] although it is not specific for cPFD.[5] The suspicion of defects of primary hemostasis (such as cPFD or VWD) could be raised by the prevalence of mucocutaneous bleedings over other types of bleedings. Global tests of primary hemostasis, such as the bleeding time and the platelet function analyzer -100 closure time are not very sensitive and specific and are therefore not very useful.[6] A two-step diagnostic strategy for cPFD is suggested.[7] The first step, based on screening tests, should help raise a diagnostic hypothesis, while the second step, based on specific tests, challenges the validity of the diagnostic hypothesis. In the first diagnostic step, laboratory tests evaluating platelet aggregation and secretion should be implemented, which are generally available in laboratories that are specialized in the diagnosis of cPFD. The second diagnostic step involves many heterogeneous laboratory tests, such as flow cytometry, western blot, immunoprecipitation analyses, immunofluorescence, measurement of platelet granule content, measurement of platelet eicosanoids, electron microscopy, DNA analysis, ligand binding assays, and many others, which, due to their heterogeneity and complexity, may not all be available even in specialized centers. A DNA-based diagnostic approach has a potentially very important role in the investigation of patients with cPFD.

The complexity of the diagnostic work-up for cPFD accounts for the paucity of specialized centers and for the inability to reach a definite diagnosis in about 40% of patients presenting with congenital mucocutaneous bleedings not associated with known abnormalities of von Willebrand factor or other plasmatic adhesive proteins that are involved in platelet adhesion and/or platelet aggregation. To improve our diagnostic performance, we think that an effort should be made to bring together all the centers that are devoted to the diagnosis of cPFD, independently of the complexity and variety of laboratory techniques that are available in each of them.

With this aim in mind, it has been recently organized a diagnostic network for cPFD (ReDIP, *Rete Diagnostica Italiana per Piastrinopatie congenite*) in Italy. ReDIP aims at taking a census of as many as possible Italian centers that are involved in the diagnosis of cPFD and favor their interaction and collaboration. An independent ReDIP website has been created to facilitate contacts and exchange of information: https://www.retepiastrinopatie.it/. The smooth operation of ReDIP not only will allow the identification of a greater number of cPFD patients and, consequently, their improved clinical management, but it will also act as a catalyst for the cultural growth of all participating centers, aligning their activities with state-of-the-art standards, and increase the awareness of cPFD in the medical community as well as in the general population at large.

References

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