Introductory preface for the special series “sticky platelet syndrome”

Thromboembolism, both arterial and venous, undoubtedly represents a pressuring medical problem, affecting a significant portion of the overall population and leading to unneglectable morbidity, mortality, and social and economic consequences. Data from the last two decades show that it is, as the underlying mechanism of myocardial infarction, ischemic stroke, and venous occlusion, responsible for a quarter of all deaths worldwide and is on the rise, particularly in developed countries (1).

The underlying prothrombotic changes were and remain a significant focus of hemostasis research since its beginning in the 19th century. The main components involved in the thrombus formation—plasmatic coagulation factors, vessel wall, and blood cells, including platelets—and the direct impact of their quantitative and qualitative disorders were identified in its first phase in the late 19th and early 20th century (2). The disorders of plasmatic coagulation factors and their regulators received the most interest and recognition. Since the pioneering description of inherited antithrombin deficiency by Egeberg in the 1960s, several clinically relevant disorders, both inherited and acquired, have been identified and become a cornerstone for thrombophilia screening and thrombotic risk assessment in routine clinical practice. On the other hand, the platelet disorders remained, perhaps except for quantitative changes in myeloproliferative disorders, relatively out of the spotlight. However, platelets were proven to play an essential and complex role in hemostasis; not only do they directly participate in the thrombus formation, but they regulate and mediate the involvement of the hemostatic, vascular, immune, and inflammatory systems (3). Thus, a plausible conclusion is to consider platelet function disorders as other prothrombotic conditions.

Platelet hyperaggregability to adenosine diphosphate and/or epinephrine, nicknamed sticky platelet syndrome (SPS) by one of its co-founders and the focus of the presented special series, represents one of few functional platelet disorders related to the increased risk of thromboembolism. Since its initial description by Holiday and Mammen in the 1980s, the growing clinical evidence, albeit restricted to selected subpopulations (European ancestry, individuals suffering from thromboembolism, women with unexplained gestational complications), linked the disorder with a variety of thromboembolic events—from common ones, such as myocardial infarction, ischemic stroke, venous thrombosis of lower extremities with/without pulmonary embolism, to less frequent, including retinal vein occlusion, renal thrombosis related to kidney transplantation, and gestational vascular complications including miscarriage and fetal growth restriction (4). Clinical data suggested the particular importance of the syndrome for the subgroup of pregnant women. The addition of antiplatelet therapy, predominantly with low-dose acetylsalicylic acid, frequently led to a surprising improvement in the affected individuals’ condition. However, despite unequivocal clinical observations, several unresolved and discussable issues, particularly the lack of broader population studies, conflicting results of genetic studies, the ambiguously addressed contribution of other prothrombotic conditions and diseases to platelet reactivity, reliability, and reproducibility of platelet aggregation testing, and validation of diagnostic criteria, remain the sources of skepticism towards the syndrome. The special series aims to address some of the problems.

In their contribution, Dr. Soto-Vega and colleagues share the unique, over the 20-year-long experience with the SPS in the Mexican Mestizos (5). Focusing on a different population than in other published studies, they provide a broader perspective on the syndrome and open the intriguing question of possible ethnic differences in its epidemiology, clinics, and management. The co-existence with other prothrombotic conditions is stressed as well.

Dr. Kessler and collaborators provide expert insight into platelet aggregometry, a key and perhaps most challenging issue on the SPS (6). They outline the common pitfalls and stress the importance of the preanalytical phase. Through their own experience, they challenge the traditional approach to platelet hyperaggregability evaluation. They provide daring but stimulating arguments for the re-evaluation of historically established laboratory criteria, questioning the repeated testing, agonist concentrations, cut-off values, and normal ranges for specific subgroups.

I am deeply grateful to all authors for their contributions, which certainly will stimulate the discussion on the role of platelets in thrombophilia. Besides them, I would like to express special gratitude to the late Professor Peter Kubisz, the hemostasis expert with a career-long interest in platelet disorders, an avid supporter of platelet importance in thrombophilic conditions, and an enthusiastic advocate of the syndrome. He was the original initiator and editor of the series. I dedicate the series on the SPS to his memory.
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Footnote

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