

## Personal reflections on the Sticky Platelet Syndrome (SPS)

Peter Kubisz, prof., M.D., D.Sc

*Once a platelet says to his comrades: lets aggregate, let it be our way. Though the clinicians liked our clotting, we can not all the time, it is not our wish! It is our destiny. No one understands us.*

G.V. Born

**S**ticky platelet syndrome (SPS) is a thrombophilic thrombocytopathy with familial occurrence and autosomal dominant trait, characterized by an increased in vitro platelet aggregation in response to low concentrations of adenosine diphosphate (ADP) and/or epinephrine (EPI).<sup>1,2</sup> Sticky platelet syndrome was for the first time publicly described as a separate clinical syndrome by Holiday and associates at the Ninth International Joint Conference on Stroke and Cerebral Circulation in Arizona in 1983.<sup>3</sup> The relation between platelet hyperaggregability and ischemic stroke was initially recognized by al-Mefty et al in 1979.<sup>4</sup> In 1984, Mammen treated a female patient who suffered from myocardial infarction during the third semester of her first gravidity and in whom the extensive laboratory testing of hemostasis revealed no abnormalities except in vitro increased platelet aggregation after ADP and EPI.<sup>5</sup> In the following years, Mammen and associates published their studies on a larger series of patients, defined generally accepted laboratory diagnostic criteria, and proposed two types (I and II) of the syndrome.<sup>5-8</sup> In the late 2000s, Mühlfeld et al<sup>9</sup> and El-

Amm et al<sup>10</sup> regarded the syndrome as a possible cause of thrombotic complications and impaired function of the graft in kidney transplantation. Throughout the years, several studies focused on the etiology and pathogenesis of the syndrome, but they had failed to fully reveal the genetic basis underlying the syndrome.<sup>11</sup> The Sticky platelet syndrome research interested doctors from different fields of medicine in recent years (cardiology, surgery, and ophthalmology).<sup>12-14</sup>

In 2002 were introduced methods for the diagnosis of sticky platelet syndrome in Martin (The National Center of Hemostasis and Thrombosis in Slovakia). Currently, our Working Group devoted to each state of hemostasis systematically. However, the main emphasis is on primary hemostasis. This group composed of 11 members (Dobrotova, Holly, Chudej, Chudy, Chuda, Ivankova, Lisa, Plamenova, Stasko, Sokol and Skerenova). We appreciate international cooperation with our Czech colleagues, Danubian League against Thrombosis and Haemorrhagic Disorders (DLTH), International Society on Thrombosis and Hemostasis (ISTH) and Grupo Cooperativo Latinoamericano de Hemostasia y Trombosis (CLAHT).

Over 1500 people were examined on SPS since 2002. SPS was confirmed in 315 people. The most common clinical manifestation in our group of patients was: deep vein thrombosis, abortion, stroke, myocardial infarction, thrombophlebitis, and retinal vein occlusion. Also, we found arterial thrombosis in approximately two-thirds of

Department of Hematology and Transfusion Medicine, National Center of Hemostasis and Thrombosis, Jessenius Faculty of Medicine, Comenius University, Kollarova 2, 036 59 Martin, Slovakia

all patients with SPS (with stroke and coronary syndromes). In our population is most common SPS Type II, Type III SPS is rare. What is very interesting because in the Mexican population is dominant SPS Type III.<sup>15</sup> However, the aim of our work is not just a statistical analysis of SPS occurrence, but especially revealing its causes. It has been supposed that glycoprotein receptors on the platelet surface membrane may be involved, its abnormality leading into platelet hyperfunction. Up to now, no molecular substrate to explain the platelet hyperaggregability has been found. This being the reason why only few research groups have accepted this entity as a true thrombophilic condition. Our research had focused on GPIIIa, Gas6, and GPVI proteins. These glycoproteins were interesting because certain mutations in their genes were shown to modulate the risk of thrombosis event in humans. In our studies, we have confirmed for the first time that the SPS has probably the polygenic mode of inheritance. Each gene locus had an independent effect on a single phenotype. Therefore, hyperaggregability is a phenotypic expression of several inherited genes. There is an open question: are there genes of small or large effect? But these are the conclusions of our Working Group. Further research in this area is needed. Platelets still hiding other secrets.<sup>11</sup>

Despite several unresolved issues and likely infrequent prevalence in general population, sticky platelet syndrome seems to be a disorder relevant for clinical practice. With its affection of predominantly young adults, relation to fertility issues, familial occurrence, distinct laboratory diagnostics, and treatment.<sup>11,16</sup>

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