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A personal view of the sticky platelet syndrome.

Visión personal del síndrome de plaquetas pegajosas

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Thirty-eight years ago, in 1983, Holiday, Mammen and Gilroy employed the term sticky platelet syndrome (SPS) to describe a syndrome identified in a group of young persons with cerebral infarction and platelet hyperaggregability. By then, I was returning to my hometown in Puebla, México, after completing a post-graduate research fellowship in hematology at the Mayo Clinic in Rochester MN, where I had the chance to meet real giants of the thrombosis and hemostasis field such as Walter Bowie, William Nichols, Kenneth Mann and David Fass, among others. Despite the fact that I was not working with them, personal encounters resulted in my increasing interest in both thrombosis and hemostasis, since my attention was then focused in the hematological malignancies and bone marrow transplantation topics. I started to make some studies in thrombophilia while being back to México in 1999. Following this line, two years later, in 2001, I became familiar with the SPS and decided to make an analysis of its prevalence in my country; we published our experience one year later, in 2002. I remember very clear the reaction of Prof. Rodger Bick, by then the editor of *Clinical and Applied Thrombosis and Hemostasis (CATH)* when, after reviewing our paper, he expressed that he was pleased to accept for publication of our “excellent paper”. I have to admit that in my whole life, I have never had another so positive comment to any other paper. Professor Bick was a believer on the SPS, and a pupil of Professor Eberhard Mammen, the creator of the term SPS. Later on, I decided to continue research on the SPS despite the fact that many famous experts in coagulation, so called “clotters”, always considered the SPS as a laboratory phenomenon or artifact and not as a clinical entity. Our studies and those of other scientists working on this area have been and are still being criticized by several clotters who

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neglect the need to investigate this condition in thrombophilic persons, very frequently stemming from their inability to look for the phenotype of the condition in their laboratories. In 2011, I met in Montevideo, Uruguay another believer in the SPS, Professor Peter Kubisz, while attending a meeting organized by Ernesto Novoa and later on, in 2013, I asked him to participate in a symposium on platelets in Cancún, México, where I was able to include in an SPS symposium, both endorsers and non-endorsers of the condition. In 2015, professor KUBISZ asked me to lecture on SPS in Sarajevo, Bosnia-Herzegovina during the meeting of the Mediterranean League against Thrombosis, where I had the chance to meet another “giant clotter”, Prof. Emmanuel Favaloro, another believer in the SPS and editor of *Seminars in Thrombosis and Hemostasis*. Subsequently, Prof. Kubisz invited me to lecture again on the topic in Martin, Slovakia in 2018, where I crossed pathways again with Prof. Emmanuel Favaloro and this year I was invited again to Martin, Slovakia to make a presentation on the SPS during the XXVIIth Slovak-Czech conference in Hemostasis and Thrombosis.

As a result of our interest in the SPS and with the help of all my collaborators as well as the giant clotters which I have mentioned, I have been able to learn several pieces of information on the SPS which I will try to summarize:

The SPS is a phenotype of platelet hyperaggregability, defined by increased *in vitro* platelet aggregation after the addition of very low concentrations of adenosine diphosphate and/or epinephrine. The concentrations and dilutions of the agents have been relatively well standardized.

The genotype is currently unknown, but several observations on the genes of platelets proteins are being studied: platelet glycoprotein IIIa PLA1/A2; platelet glycoprotein 6, growth arrest specific 6, coagulation factor V, integrin subunit

beta 3, platelet endothelial aggregation receptor 1, serpin family C member 1, serpin family E member 1.

The SPS phenotype is probably the expression of genetic conditions interacting with other medical conditions or environmental factors, such as diabetes mellitus, hormonal therapy, pregnancy and others.

1. The SPS may lead into both arterial and venous thrombosis, the latter being more frequent.
2. The SPS is an hereditary autosomal dominant trait.
3. The SPS is the most frequent cause of hereditary thrombophilia in México and probably in other countries.
4. Patients with the SPS have been identified and treated in all continents of the world.
5. The SPS is a frequent cause on miscarriages and obstetric complications
6. The SPS usually needs another thrombophilic condition to fully express as a thrombotic episode. It has recently been described as a risk factor for thrombosis during COVID-19.
7. The hyperaggregability of the SPS reverts employing anti-platelet drugs and the re-thrombosis rate of persons with the syndrome is very low while being on treatment. Most patients revert the hyperaggregability with aspirin, but around one quarter need two antiplatelet drugs. It is therefore advisable to assess the SPS phenotype after starting the antiplatelet drug, in order to define further treatment. Treating persons with the SPS with oral anticoagulants does not reduce the re-thrombosis rate.

8. Claiming that the SPS is a non-entity indicates that it is not being assessed properly and may also be detrimental for the patients, since the consequences of defining is a simple, cheap and effective treatment, tolerated by most persons, which is the use of low-doses of aspirin and other antiplatelet drugs.

Finally, I have to state that devoting some attention to the SPS has resulted, at least for me, in the pleasure knowing very interesting people, making new friends and travelling abroad. Accordingly, the SPS is polyfacetic.

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