

Primary Thrombophilia in Mexico XIII: Localization of the Thrombotic Events in Mexican Mestizos With the Sticky Platelet Syndrome

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Brizeida Azamar-Solis, MD^{1,2}, Yahveth Cantero-Fortiz, MD^{3,4},
Juan Carlos Olivares-Gazca, MD^{1,4}, Jesús Mauricio Olivares-Gazca, MD^{1,4},
Gisela Berenice Gómez-Cruz, MD^{4,5}, Iván Murrieta-Álvarez, MD^{1,4},
Guillermo J. Ruiz-Delgado, MD, FACP^{1,2,4}, and
Guillermo J. Ruiz-Argüelles, MD, MACP, FRCP(Glasg), DSc (Hon)^{1,2,4}

Abstract

The sticky platelet syndrome (SPS) is a common cause of both arterial and venous thrombosis, being a dominant autosomal disease with qualitative platelet alterations and familial occurrence. It is characterized by platelet hyperreactivity with increased platelet aggregability in response to low concentrations of platelet agonists: epinephrine, adenosine diphosphate, or both. The clinical manifestations involve venous or arterial thrombosis, recurrent pregnancy loss, and fetal growth retardation. To analyze the localization of the thrombotic episodes in a cohort of Mexican mestizo patients with SPS. Between 1992 and 2016, 86 Mexican mestizo patients with SPS as the single thrombophilic condition were prospectively identified; all of them had a history of thrombosis. There were 15 males and 71 females. The thrombotic episodes were arterial in 26 cases and venous in 60 (70%). Arterial thrombosis was mainly pulmonary thromboembolism, whereas venous thromboses were identified most frequently in the lower limbs. Mexican mestizo population with SPS is mainly female; the type I of the condition is the most frequent; both arterial and venous thrombosis can occur, and they are mainly pulmonary embolism and lower limbs venous thrombosis, respectively.

Keywords

sticky platelet syndrome, platelet hyperaggregability, Mexican mestizo

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Introduction

The sticky platelet syndrome (SPS) is a common cause of arterial and venous thrombosis. Initially described by Holiday in 1983 at the Ninth Conference on Stroke and Cerebral Circulation in Arizona, it is the second most common hereditary thrombophilic condition in Mexican mestizos.^{1,2} Sticky platelet syndrome is an autosomal dominant disease with qualitative platelet alterations and familial occurrence characterized by platelet hyperreactivity with increased platelet aggregability in response to low concentrations of platelet agonists: epinephrine (EPI), adenosine diphosphate (ADP), or both.¹⁻⁴ The diagnosis is based on platelet aggregometry, and according to this study, there are 3 types⁵:

- Type I: Hyperaggregation after EPI and ADP.
- Type II: Hyperaggregation after EPI alone.
- Type III: Hyperaggregation after ADP alone.

Type II is the most common presentation in Caucasians, type I is frequent in Mexican mestizos,¹ whereas type III is very uncommon.^{1,4-7} The clinical manifestations involve venous and arterial thrombosis, fetal loss, and fetal growth retardation.^{1,3,6,8,9} In this study, we analyze the localization of both the arterial and venous thrombotic events in a cohort of Mexican mestizo patients with the SPS.

¹ Universidad Popular Autónoma del Estado de Puebla, Puebla, Mexico

² Laboratorios Clínicos de Puebla, Puebla, Mexico

³ Universidad de las Américas Puebla, Puebla, Mexico

⁴ Centro de Hematología y Medicina Interna de Puebla, Puebla, Mexico

⁵ Benemérita Universidad Autónoma de Puebla, Puebla, Mexico

Corresponding Author:

Guillermo J. Ruiz-Argüelles, Centro de Hematología y Medicina Interna de Puebla, 8B Sur 3710, 72530 Puebla, Mexico.

Email: gruizl@clinicaruiz.com



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Table 1. Salient Features of the 86 Patients With Sticky Platelet Syndrome and Thrombosis.

| | | Arterial (n = 26) | Venous (n = 60) | P (<.05) |
|-------------|------------|----------------------|--------------------|----------|
| Age (years) | Mean | 36.6 | 38.8 | Ns |
| | Median | 26 | 28 | Ns |
| Gender | Male (%) | 3 (3) | 12 (13) | Ns |
| | Female (%) | 23 (26) | 48 (58) | Ns |
| SPS | Type 1 (%) | 14 (16) | 42 (49) | Ns |
| | Type 2 (%) | 4 (5) | 5 (6) | Ns |
| | Type 3 (%) | 8 (9) | 13 (15) | Ns |

Abbreviations: NS, non significant; SPS, sticky platelet syndrome.

Material and Methods

We conducted a retrospective, descriptive study in a period of 30 years, at a single center (Centro de Hematología y Medicina Interna de Puebla, Puebla, Mexico). We analyzed Mexican mestizo patients with a clinical marker of primary thrombophilia and a history of thrombosis.¹ In this cohort, we recorded gender, type of SPS, type of thrombotic events, number of thrombotic events, and localization of the thrombosis (Table 1).

All patients had a proven (angiography or doppler ultrasound) thrombotic episode and one of the clinical markers of a primary thrombophilic condition^{1,5,7-11}: (a) family history of thrombosis, (b) thrombosis at uncommon anatomic locations, and (c) resistance to conventional antithrombotic therapy. The SPS was defined by specific laboratory methods described by Mammen et al,^{4,12,13} Kubisz et al,^{6,7,14} and Ruiz-Delgado et al.¹ Patients with clinical conditions related to secondary thrombophilia were excluded, as well as patients who had other inherited thrombophilic in addition to the SPS.¹⁵

Results

Based on the abovementioned criteria, we identified a cohort of 86 patients with SPS as the single thrombophilic condition; 15 (17%) were male and 71 (83%) were female. All of them were referred to our facility for evaluation after having suffered a thrombotic event and displaying at least one clinical marker of thrombophilia.^{1,11,15-18} In this cohort, we found SPS type I in 65%, type II in 10%, and type III in 25% of the patients (Tables 2 and 3). We also found that the thrombotic event was more frequently venous (70%) than arterial (30%) and that the

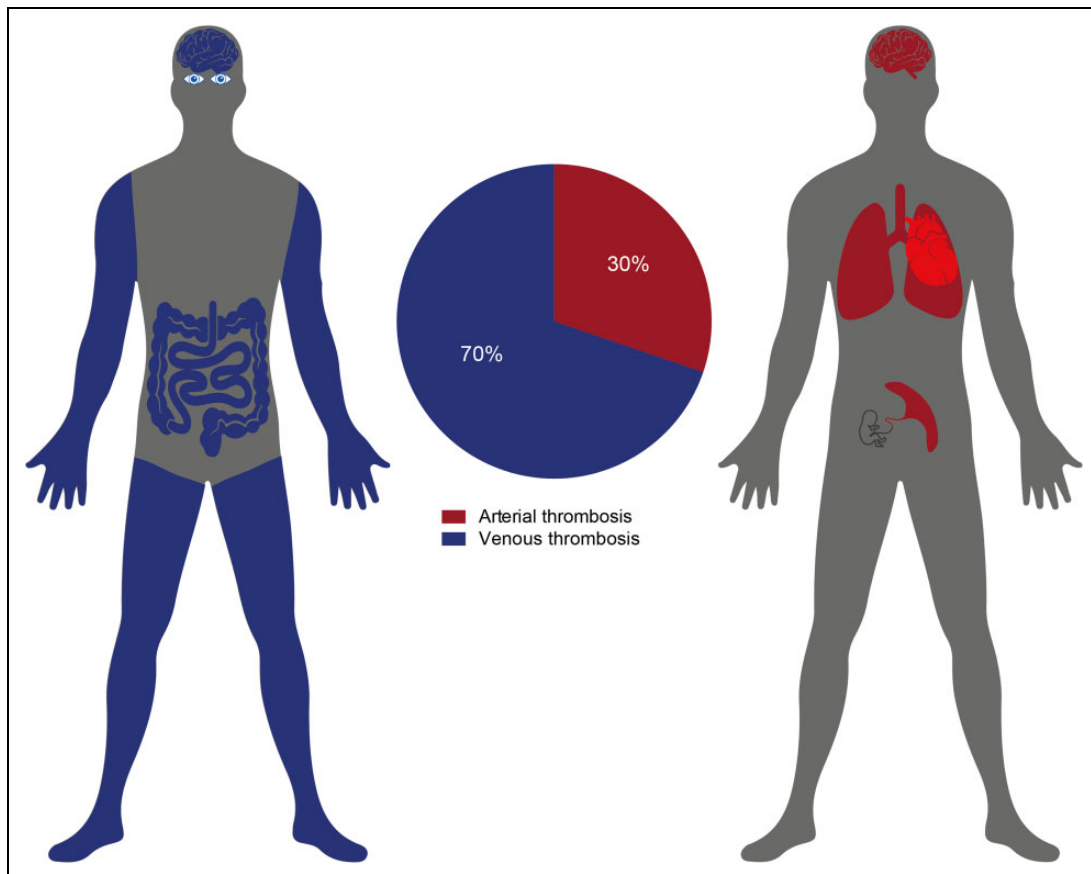


Figure 1. In the cohort of patients with the sticky platelet syndrome, the thrombotic event was more frequently venous (70%) than arterial (30%). In venous thrombosis, the localization was in lower limbs (59%), central nervous system (13%), upper limbs (8%), mesenteric veins (7%), and retinal venous thrombosis (5%), whereas in arterial thrombosis, the localizations were pulmonary embolism (50%), central nervous system (38%), placental infarction (9%), and only one case of myocardial infarction.

Table 2. Arterial and Venous Thrombosis in Patients With Sticky Platelet Syndrome According to the Subtype of the Condition.

| | | Arterial (%) | Venous (%) | P (<.05) |
|----------|-----------------|--------------|------------|----------|
| SPS type | Type 1 (n = 56) | 14 (54) | 42 (70) | Ns |
| | Type 2 (n = 9) | 4 (16) | 5 (8) | Ns |
| | Type 3 (n = 21) | 8 (30) | 13 (22) | Ns |

Abbreviations: NS, non significant; SPS, sticky platelet syndrome.

Table 3. Frequency of Thrombotic Events Among Male and Female Patients With Sticky Platelet Syndrome According to the Subtype of the Condition.

| | Arterial (n = 26) | | Venous (n = 60) | | P (<.05) |
|------------|-------------------|--------|-----------------|--------|----------|
| | Male | Female | Male | Female | |
| Type 1 (%) | 14 (25) | 3 (5) | 30 (54) | 9 (16) | Ns |
| Type 2 (%) | 1 (11) | 0 (0) | 5 (55) | 3 (34) | Ns |
| Type 3 (%) | 8 (38) | 0 (0) | 13 (62) | 0 (0) | Ns |

Abbreviation: NS, non significant.

localization of the venous thromboses were lower limbs (59%), central nervous system (13%), upper limbs (8%), mesenteric veins (7%), and retinal venous thrombosis (5%), whereas the arterial localizations were pulmonary embolism (50%), central nervous system (38%), placental infarction (9%), and only one case of myocardial infarction (see Figure 1). There was no association between the SPS type and the localization (arterial or venous) of the vaso-occlusive episode, and there was no correlation between gender and localization of the thrombosis nor between gender and the subtype of the SPS (see Tables 1 to 3).

Discussion

Sticky platelet syndrome is an autosomal inherited platelet disorder, with familial occurrence.^{7,17} Although there are certain discrepancies about the inheritance pattern, it seems that the SPS may involve various mutations resulting in the different phenotypes; however, up to now, the diagnosis relies on clinical and laboratory criteria.^{7,10} There is limited data about the prevalence of this entity in the whole population; some data indicate that up to 15% of the general population displays the phenotype of the SPS, whereas more than 60% of persons with a clinical marker of thrombophilia are found to display the SPS phenotype.^{7,11,14-19} Other authors have found that the SPS is identified in approximately 21% of unexplained arterial thrombotic episodes and 13% of unexplained venous thromboembolism^{3,13}; one of the possible reasons to explain these differences is the way to define the SPS; we and others^{1,7,11,18,19} have elected the criteria proposed by Mammen and Bick^{12,14,20-24} aiming to produce comparable results, but not all authors have employed the same criterion.¹²

Type II SPS is more frequent in Caucasians,^{2,3,25} whereas type I is the most frequent in Mexican mestizos,^{1,25} a population in which this condition is the second most frequent cause

of thrombophilia.^{1,5,11,19} It has been previously shown that the SPS may lead to both arterial and venous thromboses^{3,11,13,24} and there are scant data about the localization of these vaso-occlusive episodes.^{7,14} Kubisz et al⁷ gathered data from several publications and described the localization of the thrombotic episodes in this condition, the distribution of the thrombotic episodes being similar to the ones that we are describing here.

The thrombotic episodes stemming from SPS have been described as anticoagulant resistant,^{6,25,24} this being important in selecting the antithrombotic therapeutic approach of such patients. In a prospective study, we have shown that the rethrombosis rate in persons with SPS treated with adequate antiplatelet drugs is as low as 3.6%,²⁶ this observation supporting the need to include the investigation of the SPS in the studies of persons with suspected thrombophilia. In previous papers, we have shown that some persons with the SPS do thrombose sometimes in the presence of other thrombophilic conditions, either inherited or acquired,¹⁵ thus supporting the concept of multifactorial thrombophilia.^{15,27} In this cohort of patients, we have excluded those with other thrombophilic conditions, either inherited or acquired, in order to more precisely define the locations of the thrombotic episodes of persons with the SPS as the single thrombophilic condition.

In summary, we have described some features of the thrombotic episodes of the SPS presenting in Mexican mestizos, which are somehow different from those described in Caucasians: type I is the most frequent; it presents mainly in females; it is more frequently found in venous than in arterial thrombosis; and it is a frequent cause of lower limbs thromboses and pulmonary embolism. Additional studies are needed to define more precisely other clinical features of the SPS.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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