Peer Review File

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Reviewer Comments

Reviewer A

Comment 1: This referee is missing a clear description of the pathophysiology of the so called sticky platelet syndrome (SPS). The manuscript does not convince this referee that this SPS exists in the general population, although we see this phenomenon in myeloproliferative neoplasm.

Reply 1: A clearer description of the SPS, has been done, reference 51

Reviewer B

Comment 2: Soto-Vega et al describe the history of contributions from Mexico and the clinical manifestations of the entity "Sticky Platelet Syndrome" in Mexican patients. The article is informative and interesting, highlighting the valuable contributions from their Centre and that of Dr. Ruiz Arguelles in particular. However, the manuscript in the current (chronological recount) format lacks clarity. Most of the clinically useful information is provided in Table 2. As such, repetition of the same in the body of the text is not necessary.

I would suggest the following to improve the scientific and clinical value of the contribution: i) Revise the manuscript to include a detailed Introduction section
describing the definition of SPS and the diagnostic laboratory tests;

ii) Reduce the length of the paper by not repeating the information provided in Table 2;

iii) Consider re-writing the text without the chronological recount. A
subject based format describing clinical features, family history, clinical course
,Etc will give a better focus on SPS;

Reply 2: We appreciate the referee´s comments. We have done a review to change the article format to avoid repetition of information. We have deleted table 2

Comment 3: iv) Improve the details/clarity of information relating to co-existing thrombophilia risk factors - eg. specify whether the gene mutations were heterozygous or homozygous(lines 112, 113, 120, 130, 131);

Reply 3: We have done a review of the references concerning these lines, and it has not been possible to identify whether they refer to gene mutations heterozygous or homozygous .

Comment 4: v) Correct typographical errors - eg. Lines 309=315: many letters are missing, difficult to comprehend the message. Same applies to some References;

Reply 4: the correction has been done.

Comment 5: vi) Summarise the clinical manifestations in a Table that includes presence or absence of other thrombophilia risk factors;

Reply 5: A table has been added

Comment 6: vii) A short paragraph comparing the clinical features in the Mexican patients with those reported from the other parts of the world;
Reply 6: A table has been added

Comment 7:viii) Editorial review of the manuscript to improve the language, in particular the punctuations for better clarity and easier reading.
Reply 7: It has been done

Reviewer C
Comment 8:1. Authors should ideally have a native English writer correct the minor English Grammar and spelling issues throughout.
Reply 8: It has been done

Comment 9: 2. Some very long and difficult sentences can be split/simplified, and some sentences don't make complete sense so should be clarified; examples: Abstract: "Just like most diseases, demographic research had been mostly led in the caucasian population until the necessity of representative demographic information in the Mexican population due to the important prevalence of thrombotic events in the Mexican mestizo race, motivated the search of SPS presentation in the Mexican population."
Page 7: "A mutation in the JAK2 gene was described as acquired in patients with chronic myeloproliferative disorders and other myeloid malignancies, including polycythemia Vera (PV) and essential thrombocythemia (ET) characterized by overactive hematopoiesis and thrombosis (29,30), that's why the Ruiz-Argüelles group decided to study the JAK2 mutation in 77 patients with a clinical marker of a primary thrombophilic condition and the results showed that that the V617F mutation of the JAK2 gene was impossible to determine in any patient." Page 9: "Some authors began to study the glycoprotein IIIa PL (GP IIIa) polymorphism associated with thromboembolism (35-37), so a study was organized to analyze the association between the SPS phenotype and the platelet GP (glycoprotein) of the GPIIIa PLA1/A2 (human platelet antigen [HPA]-1a/b) gene polymorphism, 95 individuals with SPS phenotype were studied and it was found that the relationship between the GP IIIa polymorphism and the SPS was weak and not significant." And "In matters of therapeutic measures, the treatment of the SPS consist in diminishing the hyperaggregability using antiplatelet drugs like aspirin, the Ruiz-Argüelles group prospectively observed patients before and after treatment with acetylsalicylic acid (ASA) at a dose of 100 mg/d, 75 % the pathology with the ASA, while the other 25 % requires another antiplatelet drug like clopidogrel." Page 13: "The prevalence of SPS is unknown due to the lack of studies by the 2019 year only 43 published papers were found in 8 countries (51), Mexico is one of the countries that have contributed to the SPS knowledge, and it is very interesting that in Mexican mestizo population the SPS represents the second most frequent inherited thrombotic condition identified in contrast with Caucasian race, so it is necessary to look for it in patients with thrombosis in Mexico." Page 14: "Finally, once a patient is identified with SPS should start receiving the treatment which relies on attenuating the abnormal platelet hyperaggregability with antiplatelet drugs, like acetylsalicylic acid (ASA), it is an economical treatment with great results."

Reply 9: All pertinent changes have been done to make the reading of these paragraphs clearer.

Comment 10: 3. There are some text issues related to ref. 49. Please fix text on page 11, lines 309-315, and Ref 49 in the ref list.
Reply 10: The text has been corrected

Comment 11: 4. Page 6: “None of the patients presented the FV HR2 haplotype, the Cambridge, or Liverpool mutations, so these polymorphisms of the Factor V gene weren´t major contributors to the thrombophilia observed in Mexican mestizos.” Then next sentence “28% had the HR2 haplotype”
Reply 11: This has been made more clear

Comment 12: 5. Authors should utilize the same abbreviations throughout; several examples where aPCR and APCr is variably used.
6. Page 10: “APCr phenotype and Direct Oral Anticoagulants” association. Isn’t this just a case of cause? That is, patients on DOACs will potentially yield a false APCR?
Reply 12: Errors in abbreviations have been corrected

Comment 13: 7. Some abbreviations are undefined (eg CNS) and should be defined on first appearance; some abbreviations are defined multiple times (eg MTHFR)
Reply 13: The text has been checked to ensure that all abbreviations are defined in the text.

Comment 14: 8. Page 14: “SPS is an hereditary autosomal dominant” condition?
Reply 14: The mistake has been corrected

Comment 15: 9. Table 2: Author, not Autor. All author entries should be standardized to use first author then et al; also, each entry should be numerically linked to the Ref list. At-III should be AT-III; functiona should be functional; APCr and aPCR both used.
Reply 15: All the mistakes have been corrected