



HOSPITAL DE PEDIATRIA CENTRO MEDICO NACIONAL SIGLO XXI
UNIDAD DE INVESTIGACIÓN MEDICA EN EPIDEMIOLOGIA CLINICA

March 3rd, 2014

Dear editor,

Enclosed, please find the edited manuscript in Word format "**Portal vein thrombosis with protein C -S deficiency in a non-cirrhotic patient**" and Answers to reviewers.

Journal: World Journal of Hepatology

ESPS Manuscript No.: 7881

Corresponding author: Segundo Morán

Manuscript title: **Portal vein thrombosis with protein C -S deficiency in a non-cirrhotic patient**

The manuscript has been improved according to the suggestions of the reviewers:

1 Format has been updated.

Thank you for your valuable suggestions.

2 Revision has been made according to the suggestions of the reviewers:

Reviewer 1 (No 0260956)

Question 1. Regarding liver stiffness value.

In recent studies (Castera L et al. Gastroenterology 2005;128:343–350; Foucher J et al. Gut 2006;55:403–408) and EFSUMB guidelines (Ultraschall Med 2013; 34(3):238-53.) the cut-off values of liver stiffness greater than 6.8 – 7.6 kPa are highly predictive of significant fibrosis ($F \geq 2$) on biopsy in patients with chronic liver disease. You considered 7.4 kPa as normal. Please correct or clarify.

Answer: The comment of reviewer 1 is correct. The liver stiffness value in 7.4 kPa is abnormal. We corrected this mistake.

2. Some of the information that appeared in the discussion could be easily transferred to the introduction.

Answer: Changes were made when appropriate.

3. The authors should carefully read manuscript and make corrections.

a) For example: ? in "discussion" (line 8, page 7) give the abbreviation for portal vein thrombosis. We substituted the words "portal vein thrombosis" for the abbreviation PVT along the manuscript.

b) ? also give the abbreviation after first appearance of term in manuscript (transient elastography page 5, line 23)

Answer: the abbreviation for "transient elastography" TE, was corrected in all the manuscript.

c)? correct some spelling mistakes and typos (Fisher et al[7] – page 4;

Answer: a "l" was added : Fisher et al[7]

d) thromboses – page 6, line 5;

Answer : "Thromboses" was corrected for thrombosis.

e) Protein S – page 7);

Answer: capital P letter was corrected.

f)? total number of cells in the leukocyte formula does not equal 100%.

Answer : the mistake was on the eosinophils count 0%. The correct total number of cells in the leukocyte formula is neutrophils 65.6%, lymphocytes 19.0%, monocytes 15.1%, eosinophils 0.3%,

Reviewer 2 (02444774)

A slightly more detailed discussion about the epidemiology and the timing of screening for Protein C/S deficiency may be added.

Answer: The next paragraph was added:

The prevalence of protein C deficiency shown by the plasma level alone is found in 1 in 200 to 1 in 500 persons in the general population. However, many affected individuals remain asymptomatic throughout life. Protein C deficiency is present in approximately 2-5% patients presenting VTE. Severe homozygous or compound heterozygous protein C deficiency occurs in approximately 1 in 500,000 to 1 in 750,000 live births. Protein S deficiency occurs in 1.35% of the patients with venous thrombosis.

Screening the general population is not justified. There is evidence to suggest that thrombosis in unusual sites, such as cerebral sinus venous thrombosis, mesenteric vein thrombosis, portal vein thrombosis, and suprahepatic vein thrombosis (Budd–Chiari syndrome), in young individuals is also associated with inherited thrombophilia. On the basis of some studies, it seems that screening patients with unusual site thrombosis is useful.

Reviewer 3 (02462702)

A minor comment is the malignancy screening of this case was not thorough enough. The authors may briefly mention what other investigations should be done to exclude underlying malignancy.

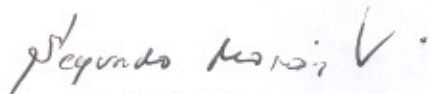
Answer:

The next paragraph was added :

An important step in PVT is to disclose malignancy. We only performed some tumoral markers (CA-19-9, ACE, AFP) but screening for JAK2V617F in order to discard myeloproliferative neoplasms and PET-scan were not performed.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,

Handwritten signature of Segundo Morán in black ink, including a checkmark at the end.

Segundo Morán, MD.

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