ANSWERING REVIEWERS

August 7, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4630-review.doc).

Title: Simultaneous intrahepatic and subgaleal hemorrhage in antiphospholipid syndrome following anticoagulation therapy

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4630

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

2 Revision has been made according to the suggestions of the reviewer

(1) Possiblity relationship between APS and transient hemorrhage

-> Some recent reports showed that APS could be correlated to a transient hemorrhagic event without anticoagulation therapy. Lupus anticoagulant-hypoprothrombinemia syndrome (LAHS) is a rare clinical entity that can occur in association with SLE. It is characterized by prolongation of the coagulation test that is not corrected by normal fresh plasma because of non-neutralizing antibodies against Factor II. Our patient did not have this abnormal laboratory finding.

(2) To emphasize the normal laboratory findings in this case, a table representing the serum data should be shown.

-> Our expression 'nomal PT INR' seems to have misunderstanding for you. It means not nomal, it means therapeutic range of PT INR. The table of Long follow-up PT INR was representing in the manuscript.

(3) The authors should carefully re-examine the photos of CT-scan, and discuss the possibility of micro-aneurysm in the liver and brain

-> We discussed the possibility of a microaneurysm in the liver and brain with radiology specialists who said that it was very unlikely.

(4) How to recognize intra-hepatic bleeding in a timely manner

-> Anticoagulant related intrahepatic bleeding is a rare entity. Patients with intrahepatic bleeding might experience right upper quadrant or epigastric pain and pain that radiates into the shoulder or flank. Fever might develop when an infection accompanies the intrahepatic hemorrhage. If a patient experience pain and/or fever during anticoagulation therapy, we should consider the possibility of abdominal bleeding such as an intrahepatic hemorrhage in any patient receiving oral anticoagulants, even though this circumstance remains unlikely. CT or US should be adopted for early diagnosis.

(5) Why a the clopidogrel was combined with the hydroxychloroquine in this case?
Why this patient no longer developed bleeding after the anticoagulation switch?

-> In studies of the bleeding risk during antithrombotic therapy, the odds ratio is generally lower for clopidogrel than warfarin, and we decided to start clopidogrel instead of warfarin[30,31]. We added hydroxychloroquine because limited data showed that it might be useful for thrombosis in patients with APS although there were no randomized controlled trials. After starting clopidogrel and hydroxychloroquine, our patients did not experience additional bleeding complications or recurrent thromboses.

3 References and typesetting were corrected

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

Sincerely yours,

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