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Format for ANSWERING REVIEWERS

June 22, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 10621-review.doc).

Title: Renal Aspergillosis after Liver Transplantation: clinical and imaging manifestations in Two Cases

Author: Xiao-Chun Meng, Ting Jiang, Shu-Hong Yi, Pei-Yi Xie, Yue-Fei Guo, Li Quan, Jing Zhou, Kang-Shun Zhu, Hong Shan

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 10621

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) **Reviewer code:** 02566971

1) Although this paper is titled "... clinical and imaging manifestations in Two Cases and review of literatures", I hardly see any literature review. Instead, the authors mentioned "According to our knowledge, RAsp has not been reported in liver transplantation recipients up to now." So this is merely a manifestation of Aspergillosis in a different organ, therefore the review of literature part can be focused on "Aspergillosis after (liver) transplantation".

Aspergillosis after liver transplantation has been reported by many researchers. The involved organs include lung, sinus, central nervous system, eyes and artery. We don't want to repeat on those fields. However, the imaging manifestations of RAsp in LT recipients still have not been described in detail. In this report, we focus on analyzing the imaging findings of RAsp in the two cases, aiming to help for its diagnosis.



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2) Several grammatical and clerical errors need further proof-reading.

We have revised the grammatical and clerical errors.

(2) **Reviewer code:** 01560498

This reviewer did not provide special suggestion.

(3) **Reviewer code:** 02730861

1) The authors need to describe in more detail the possible etiology of renal aspergillosis in their own cases.

It has been revised. In this study, RAsp may be related to haematogenous spreading in case one who had no obvious risk factors besides AOLT, and secondary to obstructive uropathy in case two who had severe urethral stenosis and mild bilateral hydronephrosis.

2) page 13, line4: The word "samphotericin B" should be changed into "amphotericin B.

It has been revised.

3) page 24, line 3 and 4: The words "(□)" should be corrected.

We did not find that word in this paper.

(4) **Reviewer code:** 02527554

1) In case one, the patient had been undergone nephrectomy because of highly suspicious of malignancy. The authors concluded that CT/MRI is useful in diagnosis of aspergillus infection. Hence, the authors should clarify the role of CT/MRI in differential diagnosis of malignancy to renal aspergillus infection?

CT and MRI are of greater value in detecting, localizing and differentiating renal lesions, but the imaging manifestations of RAsp in LT recipients still have not been described in detail. And in this study, misdiagnosis occurred in Case One because we were unfamiliar to the imaging manifestations of RAsp at that time. In this report, we focus on analyzing the imaging findings of RAsp in the two cases, aiming to help for its diagnosis. We have added the differential diagnosis of RAsp in the part of discussion.

2) How is the FK level in liver transplantation of the author's institute?

In our institute, the serum drug level of FK506 was controlled in the range of 10~13 ng/ml within 6 months after LT operation, 8~10ng/ml from 6 months to 1 year after operation and 6~8 ng/ml more than 1 year after operation.

3) Is there any serum data regarding aspergillus infection such as galactomannan test?

There was no serum data regarding aspergillus infection for the two cases, because our institute did not carried out those tests at that time.

4) Although these two cases were successful treated by surgical intervention, the authors should review and recommend on the timing of surgical treatment? For example, surgical intervention followed by antifungal failure or surgical resection first followed by adjuvant antifungal treatment.

Generally, once RAsp has been diagnosed, reversal immunosuppression is crucial for the treatment. Corticosteroids and immunosuppressive agents should be stopped immediately. Then, systemic antifungal therapy is routinely administrated. However, for the recipients after solid organ transplantation, we are obliged to deliberate over the risk of using the conservative treatment as the main treatment strategy, due to the high mortality rate of invasive aspergillosis. According to previous researches, for patients with local focus or unilateral multi-foci, radical or partial nephrectomy could be effective for reducing the risk of dissemination and mortality; And for patients with bilateral multi-foci or focus in the solitary kidney, surgical drainage with long-term antifungal therapy might be an acceptable alternative to bilateral or solitary kidney nephrectomy. In this study, both of the cases were successful treated by surgical resection followed by adjuvant antifungal treatment. They all recovered well and did not present any evidence of aspergillosis progression or dissemination more than one year after the operation, although bilateral RAsp occurred in Case Two and only the left kidney was removed. So, we want to recommend surgical resection first followed by adjuvant antifungal treatment for RAsp in liver transplant recipients. We have added that opinion in the part of discussion.

3 References and typesetting were corrected

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



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