

Current perspectives on the role of liver transplantation for Langerhans cell histiocytosis: A Narrative Review

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Dear Reviewers and Editors,

Many thanks for your valuable comments regarding our article entitled. We appreciate your interest and precious time spent in going through our article. We have now revised our manuscript taking in to account the comments, critiques and questions highlighted in your reviews. We believe that the revised manuscript now reads well and fulfils the requirements for publication in World Journal of Gastroenterology. If you have any further queries or comments, please do not hesitate to contact us.

Kind Regards

Thank you

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Reviewer #1:

Specific Comments to Authors: This paper entitled “CURRENT PERSPECTIVES ON THE ROLE OF LIVER TRANSPLANTATION FOR LANGERHANS CELL HISTIOCYTOSIS” is useful for the management and treatment of LCH patients involving Liver. Considering the outcomes of liver transplantation (LT), LT can be the mainstay in the management of some LCH patients. I agree to the role of LT in this paper.

Reply: We sincerely thank the reviewer for the comments.

Reviewer #2:

Specific Comments to Authors: Thank you for inviting me to evaluate the review titled “Current Perspectives on the Liver Transplantation for Langerhans Cell Histiocytosis”. It is an interesting paper, which summarizes the current evidence and discusses the practical & ethical aspects of the role of liver transplantation in the management of langerhans cell histiocytosis, meanwhile shows the author’s experience in treating this disease. Liver involvement in langerhans cell histiocytosis is very rare, the information in this review is helpful to clinical communities. The paper is well arranged and the logic is clear, and. The cited literature is comprehensive and modern. The provided figure and tables are well composed and understandable. The quality of language of the manuscript is quite acceptable

for me. So, I recommend to you that this manuscript should be accepted. There are some advices for author:

1) The characteristic pathological changes in the Figure are marked by arrows;

A: We thank the reviewer for the comments. As suggested by the reviewer, the figure has been updated with arrows

2) The sentence ” Liver is involved in 20-60% of patients with LCH” under LIVER INVOLVMENT IN LCH, 20-60% should be 20%-60

A: As suggested by the reviewer, the typo has been corrected.

Reviewer #3:

Specific Comments to Authors: The authors show the minireview of the liver transplantation for LCH. The review is so interesting, however, I have some concerns.

1. Which review is this, narrative or systematic? If so, please add that in the title.

A: Thank you for the comments. As advised by the reviewer, we have now edited the title.

2. What do you think is the liver transplantation effective for musculoskeletal LCH? Please discuss that citing following articles. Hashimoto K, Nishimura S, Sakata N, Inoue M, Sawada A, Akagi M. Treatment Outcomes of Langerhans Cell Histiocytosis: A Retrospective Study.

Medicina (Kaunas). 2021 Apr 7;57(4):356. doi: 10.3390/medicina57040356. PMID: 33917120; PMCID: PMC8067819. Hashimoto K, Nishimura S, Sakata N, Inoue M, Sawada A, Akagi M. Characterization of PD-1/PD-L1 immune checkpoint expression in the pathogenesis of musculoskeletal Langerhans cell histiocytosis: A retrospective study. Medicine (Baltimore). 2021 Oct 29;100(43):e27650. doi: 10.1097/MD.00000000000027650. PMID: 34713856; PMCID: PMC8556058. What do you think immune therapy is effective after the liver transplantation? Please discuss that citing the following article. Hashimoto K, Nishimura S, Ito T, Akagi M. Characterization of PD-1/PD-L1 immune checkpoint expression in soft tissue sarcomas. Eur J Histochem. 2021 Jul 2;65(3):3203. doi: 10.4081/ejh.2021.3203. PMID: 34218652; PMCID: PMC8273625.

A: Thank you very much for the pertinent comments. We have rewritten the pertinent section of the manuscript to incorporate a discussion on musculoskeletal LCH and the role of immunotherapy in its treatment. We feel the paper has enriched by adding a discussion on the topic.