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Peer Review File

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Reviewer Comments

The authors of this manuscript present a single-center experience describing clinical characteristics and outcomes of a cohort of 11 patients with molecularly confirmed arginase 1 deficiency treated by deceased or living-related donor liver transplantation. The authors are following up on earlier publications describing liver transplantation in argininemia patients in smaller case series than the current work. The cohort is well described with regard to demographic and clinical characteristics and the outcome. Table 1 contains the demographic, molecular and clinical data and is well organized but would be better for the reader if the Age at operation and Current age columns were switched in sequence for a more logical flow. Table 2 provides lab data for the cohort. It is not specified in the manuscript if these values were all preoperative labs collected at a specific timepoint or under specific fasting conditions, this information would be useful. For ammonia and arginine, there is likely to be available data on multiple samples. A range would be helpful to have if that is possible. For Table 3, since the QOL score is not standard, it might be useful to have this in the main manuscript rather than supplemental so that the quantitation behind the relative measures given can be understood by the reader. Figure 1 does not add anything substantive to the manuscript and could be deleted to make space for the QOL scoring matrix. The outcome data are compelling, particularly the video of the improvements in ambulation in one of the patients post-transplant. The Discussion is appropriate but the authors' statement regarding oligodendrocyte energy metabolism that "Our electron microscope data suggested that the mitochondrial damage resulting from arginase deficiency is responsible for the impairments" is not supported by the histological data which are restricted to liver.

Comment: For Table 3, since the QOL score is not standard, it might be useful to have this in the main manuscript rather than supplemental so that the quantitation behind the relative measures given can be understood by the reader. Figure 1 does not add anything substantive to the manuscript and could be deleted to make space for the QOL scoring matrix.
Reply: Thank you for your review and constructive comments. The comments are of important guiding significance to our paper. We re-organized the manuscript following your comments. We hope the revised manuscript will meet the high standards of editorial office. According to your suggestion, we changed Fig. 1 into Fig. S1 as supplemental materials, and added the attached content of QOL Score of Table 3 into the manuscript as Table 1, so the original Table 1-3 was changed to Table 2-4.
Changes in the text: see the Tables and Figures in the manuscript.

Comment: Table 1 contains the demographic, molecular and clinical data and is well organized but would be better for the reader if the Age at operation and Current age columns were switched in sequence for a more logical flow.

Reply: The Age at operation and Current age columns were switched in the Table 2.
Changes in the text: see Table 2

Comment: Table 2 provides lab data for the cohort. It is not specified in the manuscript if these values were all preoperative labs collected at a specific timepoint or under specific fasting conditions, this information would be useful. For ammonia and arginine, there is likely to be available data on multiple samples. A range would be helpful to have if that is possible.
Reply: The laboratory data were collected during the evaluation for liver transplantation, and we added the content in the manuscript. Since the blood arginine concentration was detected once before the operation in some cases, a range of blood ammonia and arginine concentrations were collected only part of the patients.
Changes in the text: see Page 7, line19-21; Table 3

Comment: The Discussion is appropriate but the authors' statement regarding oligodendrocyte energy metabolism that "Our electron microscope data suggested that the mitochondrial damage resulting from arginase deficiency is responsible for the impairments" is not supported by the histological data which are restricted to liver.
Reply: The statement "Our electron microscope data suggested that the mitochondrial damage resulting from arginase deficiency is responsible for the impairments" was lack of evidence, we have changed the description in the manscript.
Changes in the text: see Page 11, line 15-17

The language throughout requires some editing, some suggestions are below:

Minor line edits:

Page 3, line 14 – phrase "cause this genetic disorder" should be at end of the sentence.
Reply: We have changed the sentence as advised.
Changes in the text: see Page 3, line 14-15

Page 4, line 15 – "Due to there were few studies" should be changed to "As there are few reported studies"
Reply: We have modified our text following the recommendation.
Changes in the text: see Page 4, line 15

Page 5, line 8 – "metabolism" should be replaced with metabolic.
Reply: The change is more accurate. We have modified our text as advised.
Changes in the text: see Page 5, line 8

Page 6, line 4 – "And" should be deleted at beginning of sentence.
Reply: We have deleted "And" in the manuscript.
Changes in the text: see Page 6, line 4

Page 6, line 19 – "could only walk at a close distance" is confusing. Are the authors reporting

that the patients could only walk a short distance?
Reply: Thanks for your comment. We wanted to describe the patients could only walk a short distance, so the sentence "could only walk at a close distance" was modified.
Changes in the text: see Page 6, line 19

Page 7, line 3 – "Hyperammonemia" should be hyperammonemic.
Reply: We have modified our text as advised.
Changes in the text: see Page 7, line 3

Page 7, line 5 – "were listed" should be are listed.
Reply: We have change "were" to "are".
Changes in the text: see Page 7, line 5

Page 7, line 14 – "did not further assess" should be "were not further assessed".
Reply: We have modified the sentence as advised.
Changes in the text: see Page 7, line 14-15

Page 7, line 16 – "were listed" should be "are listed".
Reply: We have change "were" to "are".
Changes in the text: see Page 7, line 16

Page 10, line 11 – "And" should be deleted at beginning of sentence.
Reply: We have deleted "And" in the manuscript.
Changes in the text: see Page 10, line 14

Page 1, line – "for" should be changed to by.
Reply: Since the specific position was not pointed that needed to be modified, we carefully revised the whole manuscript.