Response to the **Reviewers'** comments

Dear Editor and Reviewers:

On behalf of my co-authors, we are very grateful to you for <u>this</u> opportunity to revise our manuscript. <u>Furthermore</u>, we appreciate your positive and constructive comments and suggestions on our manuscript titled "Spinal canal decompression for hypertrophic neuropathy of the cauda equina with chronic inflammatory demyelinating polyradiculoneuropathy: A Case Report" (Manuscript NO.: 73396).

We have <u>carefully</u> studied <u>the</u> reviewers' comments and tried our best to revise our manuscript according to the comments; <u>revised portions</u> are marked in red in the <u>manuscript</u>. The following are the responses and revisions I have made in response to the reviewers' questions and suggestions on a <u>point</u>-by-<u>point</u> basis. Thanks again <u>for</u> the hard work of the editor and reviewers!

Response to the comments of Reviewer #1(11.24)

Comment No. 1: It is better to change the title to "Spinal canal decompression for a 13-year-boy with hypertrophic neuropathy of the cauda equina with chronic inflammatory demyelinating polyradiculoneuropathy: A Case Report".

Response: Thank you for the reminder. Because the title is limited to 18 words, we can't add words or phrases to the title. (Page 1, Lines 4–6)

Comment No. 2: Ye L et al. Childhood hypertrophic neuropathy of cauda equine. You mean by the sentence the Running title: Childhood hypertrophic neuropathy of cauda equina

Response: Yes, <u>that is</u> the Running title. We <u>apologize for</u> not mark<u>ing</u> the running title <u>clearly</u> because the article format does not require <u>it</u> to be marked. (Page 1, <u>Line 8</u>)

Comment No. 3: Is better to replace the keyword "chronic inflammatory demyelinating " by "chronic inflammatory demyelinating polyradiculoneuropathy".

Response: The <u>suggested</u> keyword reflects the content of the article <u>better.We have made</u> revisions accordingly. (Page 4, Lines 80–81)

Comment No. 4: Abstract is badly written as well as there is a huge confusion. Compulsory major revision is needed.

Response: We agree that our abstract was not clear enough to reflect the article's content; hence, we have edited the content of the abstract again. We focused especially on revising the background and conclusion sections. Thank you very much for this observation. (Page 3; Lines 53–59, 76–78)

Comment No. 5: The introduction doesn't tell us fully what is the current knowledge of the topic and why you are considered this case as a case report.

Response: We apologize for not expressing our meanings clearly. We have edited the

Introduction again to give readers a better understanding of the research background and the purpose of our case report. (Page 5, Lines 95–104)

Comment No. 6: Although the CASE PRESENTATION was described in detail, but it needs some changes as below: a. It needs a normal reference range of the CSF protein. b. Neurophysiological testing should be separated from the imaging examination. c. You should mention the dose and type of steroid and its duration. d. You didn't mention why you don't perform B-mode ultrasound for the patient.

Response: Thank <u>you</u> for the comments on the case presentation. <u>We have</u> made the following modifications respectively:

- a. We <u>apologize</u> for our negligence <u>in not</u> indicat<u>ing the normal reference</u> range of the CSF protein. We have added this information to the Case <u>presentation</u>. (Page 6, <u>Lines 138–140</u>)
- b. We <u>have</u> separated the electrophysiological testing from the imaging <u>examinations</u>. (Page 6, <u>Lines 142–151</u>; <u>Page 7</u>, <u>Lines 154–171</u>)
- c. We agree with the reviewer's suggestion to add the dose and duration of prednisone and any adverse reactions. We have described this in the child's medical treatment during the follow-up period. (Page 8, Lines 201–207)
- d. We are sorry that we may <u>not have previously</u> expressed it clearly <u>and have</u> added why the patient was not given a B-ultrasound examination. (Page 10, <u>Lines 250–254</u>)

Comment No. 7: The figures are sufficient, , good quality, and appropriateness illustrative of the paper contents. However, the following might improve them: a. You need to rewrite the figure 1 legend to be more informative taking in consideration the following; the views of the MRI Images, avoidance of the repetition of the sentence "Diffuse thickening of nerve roots both inside and outside the spinal canal is seen", and figure 1 lacks of an arrow. b. Figure 2 lacks of arrows.

Response: Taking into account these suggestions, we have made great efforts to revise the figures to make them more professional, as detailed below:

- <u>a.</u> We <u>apologize for</u> not express<u>ing</u> it clearly, <u>and</u> have rewritten the <u>Figure 1</u>_ legend and added arrow symbols. (<u>Figure 1</u>; <u>Page 17</u>, <u>Lines 408–413</u>)
- <u>b.</u> Thank <u>you</u> for <u>the reminder; we <u>have</u> added arrow symbols in <u>Figure 2.</u> (<u>Figure 2; Page 18, Line 426–428</u>)</u>

Comment No. 8: Discussion a. This sentence "Nerve root biopsy is a safe and effective method for rapid diagnosis" needs a reference. b. You say "We consider that neurological decompression is effective for hypertrophic neuropathy with hypoechoic lesions on B ultrasound" despite you didn't perform this examination. c. "nerve biopsy is a safe method to quickly establish the etiology" This is not your conclusion.

Response: Thank you for your valuable comment. We have rewritten the <u>Discussion</u> according to these suggestions.

<u>a. In line with the</u> suggest<u>ion</u> that a reference is needed here, <u>we have</u> modified th<u>is</u> statement appropriately and added a reference. (Page 1<u>1</u>, <u>Lines</u>

272-274)

<u>b. We agree</u> that B ultrasound should not be mentioned here; thank <u>you</u> for <u>this observation</u>. We have deleted the <u>information</u> related to B ultrasound in this sentence. (Page 11, <u>Lines 295–297</u>)

<u>c. We agree</u> that th<u>is</u> sentence should not be <u>in</u> our_conclusion<u>and</u> have_deleted <u>it</u> from the <u>Conclusion_(Page 12, Lines 306–309)</u>

Response to the comments of Reviewer #2(11.29)

Comment No. 1(Abstract): Conclusion should include the phrase (following an inserted comma)", even in children" at the end of the first sentence.

Response: We have revised the content of the abstract, as the reviewer has suggested. (Page 3, Line 77)

Comment No. 2(Core Tip): The first three sentences should be as follows (suggested changes are bolded and underlined): "The rare case reported here thoroughly illustrates that chronic inflammatory demyelinating polyradiculoneuropathy can result in hypertrophic neuropathy of the cauda equina in children. This case provides new insights into the management of childhood chronic inflammatory demyelinating polyradiculoneuropathy. We demonstrated that laminectomy, followed by adjunct therapy, is a safe and effective treatment of hypertrophic neuropathy of the cauda equina. At the same time, early etiological diagnosis is very important."

Response: Thank you for <u>this</u> valuable comment. The revised expression <u>reflects</u> the <u>article's</u> main idea <u>better</u>, and <u>we have made revisions accordingly. However</u>, we <u>have</u> removed the word "early" from the last sentence because <u>the disease</u> was not in the early stage when <u>the patient</u> was admitted. (Page <u>4</u>, <u>Lines 84–91</u>)

Comment No. 3(Introduction): • Second sentence should say"exceedingly rarely reported in children.

• Last two sentences of the Introduction should be deleted.

Response: Thank you for your valuable comment._We have made corrections accordingly.

- a. It <u>must</u> be emphasized that this case is extremely rare in children and deserves to be reported. <u>Therefore, we have</u> added the phrase "exceedingly rarely reported in children" <u>at</u> the end of the sentence. (Page 5, <u>Line 100-101</u>)
- b. <u>Based on your suggestion</u> that the last two sentences were redundant, we have deleted them.

Comment No. 4(History of Past Illness, and Personal and Family History): Suggest removing the word"head" and just say trauma and inherited disorders in the patient's family history.

Response: The patient's medical history has been revised based on this suggestion that it is better to delete the word "head," thank you. (Page 6, Line 122)

Comment No. 5(Physical Examination): • The fourth sentence should mention that the additional symptoms were bilateral.

- Because the patient presented with paresthesias, their distribution on physical examination should be mentioned.
- What were the results of the gait examination (e.g., tandem gait, heel-toe walking, tip toe walking, ataxia, etc.)? Did the patient need to walk with assistance?
- Any evidence of lower extremity muscle wasting or enlarged calf muscles on physical examination? Any scoliosis?

Response: Thank you for your valuable comment. We <u>have</u> made the following modifications to the <u>manuscript</u>:

- <u>a. We agree</u> that the child had bilateral symptoms <u>and</u> have modified the original sentence by adding "bilateral." (Page 6, <u>Line 131</u>)
- <u>b.</u> Thank <u>you</u> for <u>this</u> reminder. We <u>have</u> added <u>information on</u> the paresthesias <u>disturbances below the hip joint</u>. (Page 6, <u>Lines 128–130</u>)
- <u>c. Thank you for this reminder.</u> We <u>have</u> added that the child <u>had a</u> Trendelenburg gait. (Page 6, Lines 127–128)
- d. We apologize for our <u>negligence in not</u> describ<u>ing</u> the muscle status of the lower limbs. We <u>have</u> made a supplementary description of the muscle status of the lower limbs. (Page_6, <u>Line 133–134</u>)

Comment No. 6(Treatment): • Was informed consent obtained for the surgery?

- Was IRB approval necessary?
- Was continuous somatosensory evoked potential and electromyographic monitoring used during the laminectomy?
- Were high levels of stimulation used during nerve stimulation when trying to elicit a motor response?
- What was the patient's postoperative course? Was the patient stable following the operation? Any complications?

Response: Thank you for your valuable comment._We have_made the following modifications to the manuscript:

- a. Thank <u>you for this observation</u>. The operation was performed with the <u>parents'</u> <u>consent</u>, and the electronic consent form was uploaded at the time of submission.
- b. <u>Thank you for this observation</u>. <u>The hospital</u> has authorized <u>us</u> to perform this type of surgery; <u>hence</u>, the operation, in this case, did not require IRB approval.
- c. We <u>apologize</u> for our negligence <u>in not</u> describ<u>ing</u> the <u>intraoperative</u> electrophysiological monitoring. <u>We have added to the manuscript that motor and somatosensory evoked potentials. EMG monitoring were routinely performed during spinal cord surgery. (Page 7-8, <u>Lines 179-183)</u></u>
- d. We <u>apologize for not</u> express<u>ing this</u> clearly. When there was no motor response to the nerve stimulation, we didn't increase the intensity of the stimulation because we were <u>un</u>sure <u>of</u> how high the intensity of the stimulation <u>should</u> be <u>to be</u> effective. This is something we need to improve in our future work.
- e. We <u>apologize</u> <u>for not</u> describ<u>ing</u> the patient's postoperative course. The patient was stable after the operation, and there were no surgical complications. We have

Comment No. 7(Outcome and Follow-up): Was the patient still on oral steroid treatment at the 1-year follow-up visit? How long was the patient expected to remain on steroid therapy?

Response: We <u>apologize for</u> not expressing <u>this</u> clearly. <u>The patient was maintained on</u> low-dose prednisone treatment for 1 year according to the <u>Chinese guidelines</u>, and we planned the course of treatment for 1.5 years. (Page 8, <u>Lines 203–205</u>)

Comment No. 8(Discussion): • References should be cited for the various causes of hypertrophic neuropathy listed in the third sentence.

- Discussion section should be further edited to eliminate redundancy of thought (e.g., the last two sentences of the first paragraph).
- At the end of the second paragraph, the following statement is made:"Nerve root biopsy is a safe and effective method for rapid diagnosis." What method/modality is this in comparison to?
- The characteristics of CIDP and its prevalence statistics should be mentioned earlier in the Discussion section.
- All of the terms" onion stems" should be changed to "onion bulbs."
- Although the authors mentioned that "our case demonstrates that symptoms can improve even if only spinal canal decompression is performed," there should be some mention of the role that adjunct therapy played in this case.
- The comments regarding the O'Ferrall et al study in the last three sentences of the discussion did not add value to the manuscript and should therefore be removed.
- The phrase "early etiological diagnosis" is mentioned in the Core Tip but not discussed in the manuscript. What role did early etiological diagnosis play in this case? Although the patient presented 7 years after initial symptoms, was that still considered early etiological diagnosis?

Response: Thank you for your valuable comment._We <u>have</u> made the following modifications to the <u>manuscript</u>:

- a. Thank <u>you</u> for <u>this observation</u>. This statement really should be supported by references. We have added references. (Page 9, <u>Line 238</u>)
- b. We agree with the reviewer that some sentences seem redundant. Hence, we have revised the discussion section. However, we think that the two sentences the reviewer mentioned are mainly intended to express that hypertrophic cauda equina disease can cause symptoms similar to spinal stenosis and should be treated with surgery. Thus, we think we should keep it in the text. (Page 9-10, Lines 240–244)
- c. <u>We agree with the</u> reviewer that this sentence was not a precise statement and <u>did</u> <u>not convey our intended meaning</u>. <u>Hence</u>, we <u>have</u> revised the sentence. (Page 11, <u>Lines</u> 272–274)
- d. Thank you for your valuable comment._Indeed, the epidemiological figures for CIDP should have been mentioned at the beginning of the discussion, <u>and we have</u> adjusted the paragraph distribution <u>accordingly</u>. (Page 9, <u>Lines 214–219</u>)
 - e. We have revised the relevant phrases in line with this suggestion. (Page 10, Lines

259, 262)

e-f. We agree with the suggestion that the role adjunct therapy played, in this case, should be mentioned. Hence, we have added a few sentences about the importance of adjuvant therapy. (Page 12, Lines 299–303)

£g. We have revised this part of the manuscript considering the reviewer's suggestion. We originally wanted to express the argument that Spinal canal decompression must be large enough; otherwise, the treatment might not be effective. However, this argument is not relevant to the main idea of the case report; thus, we have deleted those two sentences. (Page 12, Lines 300–303)

g.h. We agree with the reviewer that the word "early" was not suitable <u>for</u> use <u>in</u> this report. Therefore, we have removed this word in the Core Tip. (Page 4, <u>Lines 88–91</u>)

Comment No. 9(Conclusion): • The first sentence should specify pediatric patients.

- The first sentence states that nerve biopsy is a safe and quick method for diagnosis. When talking about safety, did this patient have any complications or experience any adverse events from the biopsy? When talking about quickness, how long did it take to get the biopsy results? Was that length of reporting time shorter than alternative methods, and by how much shorter?
- The term"neurological" decompression should be changed to "spinal canal" decompression.
- Relieving what symptoms? Motor, sensory, both?
- The role of adjunct therapy should be briefly mentioned.

Response: Thank you for your valuable comment. We have made the following modifications to the article content:

- a. We have revised this sentence in line with the reviewer's suggestion that it is better to emphasize, 'especially in children.' (Page 12, Lines 306–309)
- <u>b.</u> Thank you for your valuable comment. The sentence about nerve biopsy did not quite fit the topic of the <u>case report; hence</u>, we <u>have</u> removed it. (Page 12, Lines 306–309)
- <u>c. We have revised this sentence in line with the reviewer's</u> suggest<u>ion</u> that it is better to select the phrase "Spinal canal_" (Page_12, <u>Line 306</u>)
- <u>d.</u> We <u>apologize for</u> not express<u>ing</u> clearly <u>that motor</u> and sensory functions were improved in this patient <u>and have</u> revised this in the <u>Conclusion</u>. (<u>Page 12, Lines</u> <u>306–309</u>)
- a.e. We agree that the role of adjunct therapy should be briefly mentioned and have revised this in the Conclusion. (Page 12, Lines 306–309)

Comment No. 10(Figure 2): The sentence"the nerve selected for biopsy" should be changed to "the nerve root of the cauda equina selected for biopsy."

Response: Thank you for your valuable comment. It's a more <u>authentic</u> expression, <u>and</u> we have revised the legend <u>accordingly</u>. (Figure 2; Page 18, <u>Line 426-428</u>)

Comment No. 11(Figure 3): All of the abbreviations should be spelled out.

Response: Thank you for your valuable comment._All the abbreviations have been spelled out. (Figure 3; Page 19, Lines 443–446).

We tried our best to improve the manuscript and <u>have</u> made some changes <u>to</u> the manuscript. These changes will not influence the content and framework of the paper, and <u>changes</u> we did not list <u>here have been</u> marked in red in <u>the</u> revised paper.

We <u>earnestly</u> appreciate <u>the Editors/Reviewers'</u> warm work and hope that the correction will meet with <u>your approval</u>.

Once again, thank you very much for your comments and suggestions.