Author’s response to reviews

Title: Architecture of the Short External Rotator Muscles of the Hip

Authors:

Kevin Parvaresh (kcparvaresh@gmail.com)
Charles Chang (charles.chang@yale.edu)
Ankur Patel (ankee1@gmail.com)
Richard Lieber (rlieber@sralab.org)
Scott Ball (stball@mail.ucsd.edu)
Samuel Ward (s1ward@ucsd.edu)

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Reviewer reports:

Shinseki Imashuku (Reviewer 1): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Major comments

This case is not rare. In this manuscript, the authors must focus more on isolated CNS-LCH lesions causing CDI (incidence, natural course, treatment response, etc.). Additionally, the most critical question is why the enlarged pituitary stalk was masqueraded as that in lymphocytic hypophysitis. Any specific and differential MRI images for the lymphocytic hypophysitis distinct from those in LCH? Lymphocytic hypophysitis is commonly associated with autoimmune polyendocrine syndrome (APS, types 1-4). How about in this case? The statement that in LCH, CNS lesion is more unusual and LCH of CNS lesion frequently manifests as anterior pituitary hormone deficiency (APHD) is not correct, which should be revised.

As followed the reviewer’s suggestion, we reorganized the paper with focus more on isolated CNS-LCH lesions causing CDI. (Discussion and Conclusion section, line 200-259, page 11-14)
Isolated HP lesion is a clinical challenge because of that neither clinical manifestation nor MRI can make a definite diagnosis until obtaining a diagnostic biopsy. The gold standard of LCH is positive histology and immunohistochemistry evidence. (Background section, line 89-94, page 6)

Because only pituitary is involved, our case did not support the diagnosis of APS.

We also updated the prevalence rate of LCH of CNS and revised the statement as the reviewer’s recommended. (Discussion and Conclusion section, line 200-209, page 11; Background section, line 72-73, page 5; Discussion and Conclusion section, line 213-214, page 12)

Thanks to the reviewer again.

Minor comments

1. negative should be negative

has corrected. (Case Presentation section, line 123, page 7)

2. the pituitary was told to be diffusely enlarged (1.3*0.8cm); what the normal or reference size?

It was the normal size. It was rewritten as concerned. (Case Presentation section, line 130, page 8)

3. It seems to be very difficult to tell from Fig.1 ab that the high signal area of the posterior pituitary had shrunk, and the enhancement of the posterior pituitary gland was obvious but still uniform.

It has been corrected in the Case presentation. (Case Presentation section, line 130-132, page 8)

4. signal of the rest of hypothalamus were not different; compared to what?

It was compared to Imaging of normal anatomical structure.

5. gene detection was recommended to exclude B-cell lymphoma; what is gene detection?

Since the biopsy confirmed it, gene detection was not done.

6. levothyroxine was given; why? Did the patient have hypothyroid status?

Late, the patient had hypopituitary function. (Case Presentation section, line 171, page 10)

7. in people with LCH; in patients with LCH?

It is in patients with LCH. This sentence was deleted. (Discussion and Conclusion section, line 202, page 11)

8. And after continued the treatment, the pituitary stalk nodular thickening was continuous enlarged; In fact, in this case no treatment (chemotherapy) was given.

Yes, it is only observed and hormone replacement treatment. It was corrected. Thanks for advice. (Discussion and Conclusion section, line 272-273, page 14-15; Abstract section, line 45, page 3)
9. typical MRI changes for lymphocytic hypophysitis; describe in detail what images are typical for the disease and not for LCH.

The difference diagnosis of isolated HP lesion and hypophysitis is a clinical challenge because of that neither clinical manifestation nor MRI can make a definite diagnosis until obtaining a diagnostic biopsy. Thus, we corrected the statement of typical MRI changes. (Discussion and Conclusion section, line 310, page 16)

10. conformed should be confirmed

it has been corrected. (Discussion and Conclusion section, line 341, page 18)

Please overwrite this text when adding your comments to the authors.

Yes, we have overwitten it.

Sema Ciftci Dogansen (Reviewer 2): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

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The authors aimed to emphasize LCH with pituitary involvement in this case presentation.

As followed the reviewer’s suggestion, we reorganized the paper with focus more on LCH with pituitary involvement. (Background section, line 72-88, page 5-6; Discussion and Conclusion section, line 200-259, page 11-14)

Comments of Reviewer

1. Title should be changed; because lymphocytic hypophysitis is among the possible diagnoses, but there are patients' characteristics such as gender, younger age, and rapid onset of the symptoms (few weeks), which makes it difficult to think about lymphocytic hypophysitis without biopsy in the first period. I think the lymphocytic hypophysitis part of the title should be removed.

The title was changed as your advice.

2. Background and discussion (which should be changed as a CONCLUSION) sections in abstract should be shortened to maximum 2-3 sentences.

They are shortened.
3. In the background section only LCH is mentioned, where appropriate one paragraph LCH is mentioned with particularly hypothalamo-pituitary involvement, one paragraph refers to hypophysitis and infiltrative diseases of the pituitary gland, and the last paragraph should specify the purpose of the case report.

We rewrite the Background section with one paragraph LCH is mentioned with particularly HP involvement (line 72-88, page 5-6), one paragraph refers to hypophysitis and infiltrative diseases of the pituitary gland (line 89-98, page 6), last paragraph specifying the purpose of the case report (line 99-109, page 6-7). Thanks for your advices.

4. It is not appropriate to give full dates in the case report section, such as May 18, September 28, however it is appropriate to perform a chronological order according to the initiation of symptoms or diagnosis date. For example; 3 months after the onset of patients' complaints or 2 months after diagnosis….

We rewrite them. (Case Presentation section, line 112/139/157, page 7/8/9)

Thanks for your advices.

5. Grammer and spelling errors should be corrected.

We rewrite them. Thanks for your advices.

6. "A provisional clinical diagnosis of Lymphocytic hypophysitis was made. He was empirically given oral DDAVP and prednisone and the symptoms were improved." It is difficult to think of this initial diagnosis directly in this clinical picture (the reasons are given in the upper part). The diagnosis was delayed, and early diagnostic biopsy should be performed at this age with these clinical and imaging findings. And also, probably, the patient underwent a large resection rather than a diagnostic biopsy because the patient subsequently became hypopituitary. Such deficiencies in the management of the patient should be given as criticisms before the conclusion section.

Yes, it is difficult to think of LYH directly in this case, it is corrected. (Case Presentation section, line 134-135, page 8)

Yes, the diagnosis was delayed. (Discussion and Conclusion section, line 363, page 19)

The patient underwent a total tumor resection, and hormone deficiencies happened. (Background section, line 80-82, page 5; Discussion and Conclusion section, line 365-366, page 19)

Thanks for your frank and sincere advice.
7. Discussion section is scattered, I think; first hypophysitis and differential diagnoses of hypophysitis should be mentioned and how they go to the diagnosis through their own patient. Then, the general characteristics of LCH should be mentioned much shorter and longer than LCH with hypothalopituitary involvement.

we reorganized the paper with focus more on LCH with pituitary involvement.

First:(Discussion and Conclusion section, line 323-338, page 17-18)

Then:(Discussion and Conclusion section, line 200-259, page 11-14)

8. In addition, a large series of articles on this subject should be included and references should be updated. Such as "Kurtulmus N et al. The pituitary gland in patients with Langerhans cell histiocytosis: a clinical and radiological evaluation, Endocrine 2015;48(3):949-956"

It has been updated. Thanks again.