Dear Lian-Sheng Ma
Company Editor-in-chief, Editorial Office
Baishideng Publising Group, Inc

We were pleased to receive your letter concerning our manuscript entitled " Submicroscopic 11p13 deletion including the ELP4 gene in a girl with language failure, intellectual disability and congenital malformations: case report and literature review" registered with the **number 57995** submitted to Word Journal clinical cases. We now enclose a revised version of this manuscript, which incorporates the excellent suggestions of the reviewers.

Science Editor's Comments

1 Scientific quality: The manuscript describes a case report of the submicroscopic 11p13 deletion including the ELP4 gene in a girl with language failure, intellectual disability and congenital malformations. The topic is within the scope of the WJCC. (1) Classification: Grade B and Grade C; (2) Summary of the Peer-Review Report: The authors indicate that their main objective is to describe a girl with dysmorphic features, intellectual disability and congenital malformations without aniridia, and with microdeletion of 11p13 involving ELP4 gene. The manuscript is very interesting. Some points require further clarification and the manuscript may benefit by adding more focused discussion about the findings. The questions raised by the reviewers should be answered; and (3) Format: There are 3 figures. A total of 18 references are cited, including 0 reference published in the last 3 years. There are no self-citations. 2 Language evaluation: Classification: Two Grades B. A language editing certificate issued by Scribendi Inc was provided. 3 Academic norms and rules: The authors provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. The written informed consent was not provided. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by PAEP, 2018 and PAPIIT IN219419, DGAPA, Universidad Nacional Autónoma de México. The topic has not previously been published in the WJCC. 5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (3) Please provide the informed consent of the treatment of the patient. 6 Re-Review: Required. 7 Recommendation: Conditional acceptance.

We provide approved grant application form.

We provide original pictures in power point.

We provide the signed informed consent document.

The patient came to us already treated surgically, the parents report that everything was done with the required guidelines. that is why we do not have consent as we do not carry out the procedure.

Reviewer's Comments

Reviewer 1

The authors indicate that their main objective is to describe a girl with dysmorphic features, intellectual disability and congenital malformations without aniridia, and with microdeletion of 11p13 involving ELP4 gene.

I found the manuscript is very interesting. Some points require further clarification and the manuscript may benefit by adding more focused discussion about the findings.

Case presentation

Line 10-12 on page 7, "(hg 19)" can be added at the end of the sentence "The gene content…… NCBI build 37." And The preceding sentence, "The reference……. (hg 19)." can be removed.

Now we changed the phrase "The reference of the human genome is NCBI 37 (hg19). The gene content of the CNVs of interest was determined with the UCSC browser based on NCBI build 37" by the phrase "<u>The gene content of the CNVs of interest was determined with the UCSC browser based on the reference of the human genome NCBI build 38 (hg38).</u>

Result section.

- The exact location of 11p13 microdeletion and LOH of Xq should be given, to be more specific nt start and nt end of the deletion and the LOH.

Now we included the exact location of 11p13 microdeletion and LOH on Xq "<u>(arr [hg38] 11p13: 31509401-31540684)x1 dn,</u> and (<u>arr [hg38] Xq25q26.3: 124585334-134039037)x2 dn,</u>" respectively.

Discussion

I suggest the authors adding further discussion on the following issues.

- Other possible etiology underlying the unusual phenotypes (cleft lip/palate and neuromigration defect including heterotopia) other than what already been said, for example, a coincidental disorder causing cleft lip/palate and heterotopia such as Baraitser–Winter cerebrofrontofacial syndrome (Verloes et al., Eur J Hum Genet. 2015; 23: 292–301).

Now we added further discussion "<u>Interestingly, the phenotypes of microcephaly, facial dysmorphia, cleft lip/ palate, neuromigration defect, and intellectual disability of our patient has been observed in the Baraitser-Winter cerebrofrontofacial syndrome 1 and 2 [OMIM 243310; BRWS1, 614583; BRWS2)][15], but the ACTB and ACTG1 genes of BRWs 1 and 2 were not involved in the deletion or duplication regions or LOH of our patient.</u>"

- Among the 6 genes with X-linked recessive inheritance, is there any gene associated with both cleft lip/palate and neuromigration abnormalities. I suggest the authors go over these 2 papers, Kasper, et al., Epilepsy & Behavior 69 (2017) 104–109 and Ge´cz, et al., Eur J Hum Genet. 2006; 14: 1233–1237.

We add a discussion with the recommended articles in the phrase of the line 1-3 from the bottom of page 7 Page 9.

The word "The researchers" is ambiguous which researchers, the authors the submitted manuscript or of which paper.

Now we add la reference "[9] in the word "The researchers"

- Page 11, Paragraph 2

Line 3-4 is redundant with Line 3-5 from the bottom of page 7, please consider rewrite it.

Line 2-6, there are 6 genes but 7 disorders mentioned, so it is not clear which disorder was associated with which gene.

Page 11, Paragraph 2, line 3-4 was rewrite with the phrase "6 of which were related to X-linked diseases (*OCRL:* Dent disease 2 and Lowe oculocerebrorenal syndrome, *AIFM1:* Cowchock syndrome, *IGSF1:* Central hypothyroidism and testicular enlargement, *GPC3:* Simpson–Golabi–Behmel syndrome (SGB), *PHF6:* Borjeson–Forssman–Lehman syndrome (BFL), *HPRT1:* Lesh Nyhan syndrome) (Figure 3)"

and la phrase from the line 3-5 from the bottom of page 7 "6 of which (*OCRL, AIFM1, IGSF1, GPC3, PHF6, HPRT1*) were related to X-linked diseases (Figure 3), such as Dent disease 2, Lowe oculocerebrorenal syndrome, Cowchock syndrome, central hypothyroidism and testicular enlargement, Simpson–Golabi–Behmel syndrome, Borjeson–Forssman–Lehman syndrome, and Lesch–Nyhan syndrome, respectively." was deleted.

A reference is needed for "Borjeson-Forssman-Lehman syndrome has been associated with cleft palate"

Now we changed the phrase of the line 1-3 from the bottom of page 7 "Four of them have been associated with intellectual disability, and Borjeson–Forssman–Lehman syndrome has been associated with cleft palate" and a reference was added "four of them have been associated with intellectual disability, *OCRL*, *AIFM1*, *PHF6* and *HPRT1* genes (HP: 0001249 in OMIM) (figure 3). The BFL syndrome has been associated with cleft lip/palate, microcephaly, band heteropia and simplified gyral cortical patterns as the case of some female due to a de novo intragenic duplication of *PFH6*[16,17], characteristics found in our patient."

Other minor comments

- "upward-sloping" were changed by "**upward-slanting**" in the text
- Author contributions "Molecular Karyotyping" was changed by "**molecular karyotyping**"

- Line 2 from the bottom of page 8, “ELPA” was corrected to “**ELP4**”

Reviewer 2

This is a case report that is interesting and useful due to the link to a chromosomal abnormality. There are two details I suggest the authors to revise. In the title, delete the “case report and literature review.” In the conclusion, delete the word “special” when referring to treatment.

Now we deleted the phrase “case report and literature review” from title and the word “special” was deleted from the text.

Sincerely yours,

Sergio A Cuevas Covarrubias
Corresponding author