Author’s response to reviews

Title: 11q23 deletion syndrome (Jacobsen syndrome) with severe bleeding: a case report

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Author’s response to reviews:

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Dr. Chinmoy Bose

Deputy Editor

Journal of Medical Case Reports

Re: JMCR-D-17-00281 11q23 deletion syndrome (Jacobsen syndrome) with severe bleeding: a case report
Dear Dr. Bose:

Thank you very much for the opportunity to submit a revised version of our manuscript “11q23 deletion syndrome (Jacobsen syndrome) with severe bleeding: a case report”. Based on the recommendations from you and the reviewers, we have worked on improving the quality of our original manuscript. We hope that this report is now fit for publication in your esteemed journal.

This revised manuscript contains the following items:

- Main text with 1407 words and 15 references
- One main figure
- Supplementary information containing 1 supplementary table.

This paper has not been published elsewhere, completely, partly, or in another form. We also declare that there is no conflict of interests over the contents and authorship of the manuscript and that there are no financial interests.

Thank you for your kind consideration.

Yours sincerely,

Yuko Ichimiya, M.D., Corresponding author

Point-by-point responses to the editor and reviewers
To Reviewer #1:

Thank you very much for your helpful comments. We report that our manuscript was successfully reorganized according to the Reviewer's advice. Below are the answers to Reviewers’ comments. Corrected parts are highlighted with a yellow marker in the revised text.

Authors should include a more precise description of the patient.

What were the genes involved in the deletion? Image of the array should be added.

Response:

We added the image of the array as Figure 2 as the Reviewer suggested. We inserted the following text: “Array comparative genomic hybridization analysis confirmed a deletion of the 13.0 Mb regions ranging from 11q24.1 to the q terminus encoding FLI1, BSX, and BARX2 (Figure 2).” (page 8, lines 114-116) “Patient had 11q deletion which include FLI1, a gene associated with dysmegakaryocytopenia, BARX 2, a candidate gene for the development of facial dysmorphism and craniosynostosis, and BSX, a gene having a role in regulating locomotor behavior.” (page 8, lines 120-124)

The authors should make a more exhaustive review of the literature

Response:

In accordance with the Reviewer’s suggestion, we carefully re-examined the literature and rechecked the supplementary materials. As the majority of patients with the prenatally diagnosed 11q23 deletion syndrome are terminated, we excluded such cases. This is the first report to review “liveborn” patients with the diagnosis of 11q23 deletion syndrome during the perinatal period. We emphasized this fact and inserted the following text: “To date, 25 liveborn patients diagnosed with 11q23 deletion syndrome during the perinatal period have been reported.” (page 9, lines 139-140) “Nine out of 25 reported cases were diagnosed prenatally and delivered, four of which had thrombocytopenia.” (page 10, lines 158-160)

Were the parents analyzed? Were the parents carriers of a chromosomal translocation?

Response:
We did not analyze the parents.

"Hemizygous deletion"?, please correct the nomenclature.

Response:

Thank you for the comment. We changed “hemizygous deletion” to “hemizygous loss” (page 5, line 71).

What do author mean with "He exhibited skull deformities", please be more specific.

Response:

We have modified the description to “He exhibited dolichocephaly with a high, prominent forehead.” (page 7, lines 96-97)

Author should enrich the discussion and not only refer " bleeding tendency" , there's a lot of genes involved in the deletion, what about of them?, discuss it please

Response:

Thank you very much. As mentioned above, we corrected our original description according to your suggestion. (page 8, lines 114-116) (page 8, lines 120-124)

To Reviewer #2:

Thank you very much for your helpful comments. We revised our manuscript according to the Reviewer's advice. We revised all the points below in accordance with your recommendations. The corrected parts have been highlighted with a yellow marker in the revised text.
Observations:

Abstract:

Introduction: 11q23 deletion syndrome, previously known as Jacobsen syndrome, is characterized by growth retardation, psychomotor retardation, facial dysmorphism, and thrombocytopenia.

Should be:

Introduction: 11q23 deletion syndrome, also known as Jacobsen syndrome, is characterized by growth retardation, psychomotor retardation, facial dysmorphism, multiple congenital abnormalities and thrombocytopenia. (Line34)

Response:

We revised this sentence as suggested. (page 3, lines 34-36)

Conclusions:

Our patient with FLI1 deletion avoided massive bleeding and serious sequela by careful management after prenatal diagnosis

Should be:

"Our patient with 11q deletion including the FLI1 gene avoided massive bleeding and serious sequela by careful" (Line55)

Response:

We modified this sentence as suggested. (page 4, lines 55-56)

Introduction

A contiguous gene syndrome, 11q23 deletion syndrome is characterized by growth retardation, psychomotor retardation, facial dysmorphism, abnormal platelet function, and thrombocytopenia.
Until the genetic region for the syndrome was found, the condition was known as Jacobsen syndrome and considered to be the same as Paris-Trousseau syndrome, which is accompanied by congenital thrombocytopenia [1].

Should be:
"A contiguous gene syndrome, 11q23 deletion syndrome, is characterized by growth retardation, psychomotor retardation, facial dysmorphism, multiple congenital abnormalities, abnormal platelet function, and thrombocytopenia. The syndrome is also known as Jacobsen syndrome and congenital thrombocytopenia/thrombocytopathy observed in most affected patients is considered to be the same as Paris-Trousseau syndrome [1]." (Line 65)

Response:
We changed the first paragraph in the Introduction section as suggested. (page 5, lines 65-70)

chromosome 11: 46,XY, add (11) (q23) was found.

unless the deletion is a consequence of a translocation and there is part of an unknown chromosome attached to the deleted chromosome 11q

Should be: "46,XY, del(11) (q23->qter)" (Line 88)

Response:
We revised this phrase as suggested. (page 6, line 88)

He exhibited skull deformities, facial asymmetry, low-set ears, inguinal hernia, flat 96 feet, and crowded toes (Figure 1).
Figure 1 is missing, add a figure 1 or eliminate and change figure 2 into figure 1

Response:

We changed Figure 2 into Figure 1, and added a new image of the array as Figure 2.