Peer Review File
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Reviewer A

This is a very interesting short case report on a child with a large deletion involving the short arm of chromosome 10 and the role that the palliative care team has had in her medical management. I really appreciated the different perspectives provided, including those of the foster parents, who are clearly very involved in their daughter's care.
Some suggestions to improve the manuscript:
1) Additional editing for language and clarity.
2) Add the size of the deletion (21 Mb) to the abstract. Note that at least one similarly large deletion has been reported in the literature that was not cited in your manuscript, although CMA was not completed (see Benetti et al., 2009, PMID: 19022243).
3) In the description of the chromosome 10 abnormality, utilize the current ISCN standard nomenclature to describe the patient's genetic results:
46,XX,del(10)(p12).arr[GRCh37] 10p15.3p12.31(136361_21057840)x1 dn
4) It would be interesting to have a more detailed discussion point on how the PPC team is involved in coordinating and streamlining care between multiple different specialties for children with such complex medical needs to simplify management of many conditions and ease this burden for the family.

Comment 1: Additional editing for language and clarity.
Reply 1: Thanks for this comment. Changes in the text were made and the text has been revised also by a reviewer.

Comment 2: Add the size of the deletion (21 Mb) to the abstract. Note that at least one similarly large deletion has been reported in the literature that was not cited in your manuscript, although CMA was not completed (see Benetti et al., 2009, PMID: 19022243).

Reply 2: Thanks for these suggestions. the size of the deletion has been added at the beginning of the abstract. In the discussion we cite now the case report described by Benetti et al.
Changes in the text: Abstract line 52; discussione lines 219-223

Comment 3: In the description of the chromosome 10 abnormality, utilize the current ISCN standard nomenclature to describe the patient's genetic results:
46,XX,del(10)(p12).arr[GRCh37] 10p15.3p12.31(136361_21057840)x1 dn

Reply 3: Thank you for your observation. We replaced the description of the chromosome 10 abnormality with the current ISCN nomenclature.
Changes in the text: case presentation, line 161

Comment 4: It would be interesting to have a more detailed discussion point on how the PPC team is involved in coordinating and streamlining care between multiple different specialties for children with such complex medical needs to simplify

management of many conditions and ease this burden for the family.

Reply 4 :
Changes in the text have been done (lines 254-258; 232-235) in order to explain the coordination role done by PPC.

Reviewer B

This case report is well written, clinical description is detailed and the uncertainty about the overall prognosis is clearly explained.
However, the authors should stress earlier in their presentation the concept of Complex Chronic Conditions and discuss more about it with references to Feudtner's publications for instance.
In fact, this case report stresses the need for children with CCC especially with severe neurological impairment/PIMD/polyhandicap to have an efficient case manager/coordinator that may be the PPC team. This should be more discussed.

Reply: Thank you for these suggestions. We added reference to the CCC in the introduction and we have explored the concept further in the discussion. We also added some consideration in the discussion.
Changes in the text: introduction line 127; Discussion: line 233, lines 254-266

Reviewer C

The paper is a case report of an infant with a large terminal deletion of the short arm (p) of chromosome 10 and multiple congenital anomalies, including intellectual disability. It describes the important role of pediatric palliative care (PPC) in the management of this infant, and similarly affected children.
The authors refer to the condition as “distal monosomy 10 p syndrome”. This is a disorder rather than a syndrome, as the phenotype is variable depending on the size and location of the deletion. Moreover, OMIM does not list it as a syndrome.
A geneticist would be more equipped to address this issue.
Chromosome 10, monosomy 10p is a rare chromosomal disorder with deletion of the terminal portion of the short arm (p) of chromosome 10. As such, the title of the paper is a bit confusing as it says “large deletion of chromosome 10”. It is probably more appropriate to say “a large deletion of the short arm (p) of chromosome 10”.
In my opinion, his patient fits the diagnosis of HDR (Barakat) syndrome [Hypoparathytoidism, Deafness, Renal disease and deletions in chromosome 10p14 or mutations in the GATA3 gene]. The phenotypic heterogeneity seen in the Barakat syndrome is probably due to variability of expression and incomplete penetrance of GATA3 mutations. The fact that GATA3 defects were not detected in over 9% of the studied patients, leaves open the possibility of the presence of other gene defects associated with this disorder (Barakat AJ, Raygada M, Rennert OM. Barakat syndrome revisited. Am J Med Genet. 2018; 176: 1341). Furthermore, HDR syndrome can be associated with partial monosomy 10p (Lichtner P, et al. An HDR (hypoparathyroidism, deafness, renal dysplasia) syndrome locus maps distal to the

DiGeorge syndrome region on 10p13/14. J Med Genet 2000; 37:33).
In my opinion this paper is worth publishing after the following modifications:
1. The paper needs editing. Although table 1 is clear, the sequence in the case presentation needs to be better organized, and some information needs to be more accurate. Examples:
Line 108: says "left mild hydroureteronephrosis and no renal anomalies". The authors probably mean "mild left hydroureteronephrosis, but no other renal anomalies".
Line 141: "J's situation was slightly improving". Which situation are the authors referring to?
Line 143: "Milestones remained severely delayed": which milestones?
Line 145: Some motor milestones were achieved". Sitting and transferring objects from one hand to the other. These milestones are achieved much earlier than age 5 years.
Line 250: The reference listing should be consistent. Reference 1 is listed in a different format than the other references.
2. In my opinion, the clinical and genetic information should be presented, but the title of the paper suggests that the stress should be on the role of the PPC in helping these high need children to improve. The disciplines involved and the methods used to help these patients to improve each of their problems should be discussed in detail to stress the impact of PPC on affected children to try to help them reach their potential.

Answers

Comment 1:The authors refer to the condition as "distal monosomy 10 p syndrome". This is a disorder rather than a syndrome, as the phenotype is variable depending on the size and location of the deletion. Moreover, OMIM does not list it as a syndrome. A geneticist would be more equipped to address this issue.
Reply 1: Thank you for your observation. We have verified that syndrome is not appropriate
Changes in the text: We eliminated the word syndrome in the manuscript (lines 54, 134)

Comment 2: Chromosome 10, monosomy 10p is a rare chromosomal disorder with deletion of the terminal portion of the short arm (p) of chromosome 10. As such, the title of the paper is a bit confusing as it says "large deletion of chromosome 10". It is probably more appropriate to say "a large deletion of the short arm (p) of chromosome 10".
Reply 2: We have taken the suggestion and changed the title
Changes in the text: title **Early pediatric palliative care involvement in a child with a large deletion of the short arm (p) of chromosome 10: a case report**

Comment 3: In my opinion, his patient fits the diagnosis of HDR (Barakat) syndrome [Hypoparathytoidism, Deafness, Renal disease and deletions in chromosome 10p14 or mutations in the GATA3 gene]. The phenotypic heterogeneity seen in the Barakat syndrome is probably due to variability of expression and incomplete penetrance of GATA3 mutations. The fact that GATA3 defects were not detected in over 9% of the studied patients, leaves open the possibility of the presence of other gene defects associated with this disorder (Barakat AJ, Raygada M, Rennert OM. Barakat syndrome revisited. Am J Med Genet. 2018; 176: 1341). Furthermore, HDR

syndrome can be associated with partial monosomy 10p (Lichtner P, et al. An HDR (hypoparathyroidism, deafness, renal dysplasia) syndrome locus maps distal to the DiGeorge syndrome region on 10p13/14. J Med Genet 2000; 37:33).

Reply to comment 3: We discussed the issue collegially. Although the child has the characteristics of Barakat syndrome, we cannot define his condition as Barakay syndrome as our patient carries a large deletion that encompasses many critical regions involved in different syndromes.

Comment 4: The paper needs editing. Although table 1 is clear, the sequence in the case presentation needs to be better organized, and some information needs to be more accurate. Examples: Line 108: says "left mild hydroureteronephrosis and no renal anomalies". The authors probably mean "mild left hydroureteronephrosis, but no other renal anomalies".
Reply to comment 4: Corrections have been made.
Changes in the text: lines 150-151, 179-184.

Comment 5. Line 141: "J's situation was slightly improving". Which situation are the authors referring to?
Reply 5: Thanks for this remark. We decided to modify this sentence to "At 5 years of age, her medical condition is controlled and well managed." in the abstract and to discuss in further details in the table and in the "presentation of the case" section the developmental achievements that have been reached by the girl in the last years thanks to the dedication of the rehabilitation and the efforts done by the foster family, which allowed to J. a better integration in the social activities and in the school.
Changes in the text: abstract line 70-71; case presentation lines 185-187

Comment 6: Line 143: "Milestones remained severely delayed": which milestones?
Reply 6: We modified the sentences and clarified that.
We modified the sentence as followed: Neurological evaluation still showed a severe global psychomotor retardation. Spontaneous movements were still mainly jerky, and no fine motor skill was developed. However, muscular hypotonia had improved and some motor milestones were achieved (even if later in life): she was able to sit with support and walk with a medial walker for a few months, she started to slither but no crawling, she transferred objects between hands and to the mouth, she attended regularly the kindergarten, and enjoyed her peers. She also presented great difficulties in expressive speech but, thanks to weekly speech therapy starting from 3.5 years, she was able to communicate disappointment, pain or distress using augmentative and alternative communication.
Changes in the text: case presentation, lines 189-196

Comment 7: Line 145: Some motor milestones were achieved". Sitting and transferring objects from one hand to the other. These milestones are achieved much earlier than age 5 years.
Reply 7: Changes in the text were done accordingly and are listed in the previous paragraph reported in comment 6

Comment 8: Line 250: The reference listing should be consistent. Reference 1 is

listed in a different format than the other references.
Reply 8: Thank you for the comment. We corrected the format of reference 1.

Comment 9: In my opinion, the clinical and genetic information should be presented, but the title of the paper suggests that the stress should be on the role of the PPC in helping these high need children to improve. The disciplines involved and the methods used to help these patients to improve each of their problems should be discussed in detail to stress the impact of PPC on affected children to try to help them reach their potential.
Reply 9: we collected different recommendation in regard of the title of this case from different reviewers and we decided to leave it as **Early pediatric palliative care involvement in a child with a large deletion of the short arm (p) of chromosome 10: a case report** in order to give voice to both genetic and PPC perspectives. The PPC service role and intervention are now presented in a deeper way in the text and especially in the discussion section giving a stronger description of the discussion we had with parents in regard to the illness trajectory and decision making process and the focus on QoL.
Changes in the text:

Reviewer D

This is an interesting case report and it was nice to see that you have followed the child now for 5 years and to see the developmental progression. The writing is a little difficult to follow at times and some of the words/phrases used are confusing, and I have made editorial revisions in the attached word document.
My main critique is that there is very little description of the family's goals for their child and the rationale for when and why interventions were pursued. Could you describe your PPC model? What discussions were had with the family/foster family about the child's prognosis (including uncertainty)?

Given that the family opted for interventions, it seems they wanted to give the baby a chance and were accepting of severe developmental delays. Was the family offered the option to NOT pursue invasive interventions such as cardiac surgery? How do you typically approach these cases at your center?

I would also argue that while you cannot prognosticate with certainty given the rarity of this condition, there are many things you can tell families. You state that certain clinical features have been described with certain regions of 10p and that this child has a very large deletion so you cannot say which genes were involved? Given that his deletion is large, I would argue that you say that this child most definitely will have the clinical features described in 10p monosomy and may even be more severely affected (as his developmental progression has shown). Again, it would be nice to understand what the family was told about the prognosis and how they were counseled about interventions.
It is also unclear why the child is in foster care? Is this an immigrant family from

China who brought the child to your clinic but was unable to care for the child? Please clarify.

Observation 1:This is an interesting case report and it was nice to see that you have followed the child now for 5 years and to see the developmental progression. The writing is a little difficult to follow at times and some of the words/phrases used are confusing, and I have made editorial revisions in the attached word document.
My main critique is that there is very little description of the family's goals for their child and the rationale for when and why interventions were pursued. Could you describe your PPC model? What discussions were had with the family/foster family about the child's prognosis (including uncertainty)?
Reply 1: Thanks for your questions. The PPC team met the native family for the first time during J. admission to our hospital. On that occasion, a meeting was held by the PPC team with the parents and doctors who were treating the child. A Pediatric palliativist clinician introduced and explained the role of the PPC service, explaining all the professionals involved and the different supports offered to children and their families. During that meeting the concept of uncertain prognosis was explored. Precisely because of the uncertain prognosis in a child with complex chronic condition, the importance of a comprehensive care has been emphasized and PPC services were proposed to the J. and his family. The different treatment options were also explained (i.e. invasive vs non-invasive treatments).
We also specified why cardiac surgery was postponed and we add some information about our PPC model.
Changes in the text: lines 168, 169-172, 177-179; 127-131, 233-236, 249-259

Comment 2: Given that the family opted for interventions, it seems they wanted to give the baby a chance and were accepting of severe developmental delays. Was the family offered the option to NOT pursue invasive interventions such as cardiac surgery? How do you typically approach these cases at your center?
Reply 2: Thank you for your question. Of course this option was discussed with the family and the multidisciplinary team (cardiology and cardiac surgeons): the cardiac surgery intervention was seen and perceived by the family as a possibility with a low risk surgery to give to the child a better QoL in perspective as it was a single intervention that can lead to a reduction of O2 dependence.

Comment 3: I would also argue that while you cannot prognosticate with certainty given the rarity of this condition, there are many things you can tell families. You state that certain clinical features have been described with certain regions of 10p and that this child has a very large deletion so you cannot say which genes were involved? Given that his deletion is large, I would argue that you say that this child most definitely will have the clinical features described in 10p monosomy and may even be more severely affected (as his developmental progression has shown). Again, it would be nice to understand what the family was told about the prognosis and how they were counseled about interventions.
Reply 3: Thank you for the observation. We accepted the suggestions.
Changes in the text: abstract 58-59, case presentation lines 168-172, 177-179

Comment 4: It is also unclear why the child is in foster care? Is this an immigrant family from China who brought the child to your clinic but was unable to care for the child? Please clarify.

Reply: The native family (immigrant family from China) due to the complexity of the child management, even if the PPC team had offered all the support it could, decided not to continue to take care of the baby and place her in foster care.
This precisation has been added in the case description.
Changes in the text: case presentation lines 168-172

Reviewer E

overall - keep the same tense especially in the case presentation.
Abstract line 40 - there are studies on this in pediatric and data to suggest how this is beneficial. I would encourage the authors to include those.
Case presentation line 94 should be presented with
line 98 measures should be measurements
Line 135 - this paragraph does not read well. I would suggest having it in chronological order.
Line 146 grammar and spelling errors
Line 147 - say thanks twice, please rephrase

Comment 1: overall - keep the same tense especially in the case presentation.
Reply 1: We made corrections

Comment 2: Abstract line 40 - there are studies on this in pediatric and data to suggest how this is beneficial. I would encourage the authors to include those.
Reply 2: Thanks for the suggestion: we added this in the text.
Changes in the text: Discussion lines 237-239

Comment 3: Case presentation line 94 should be presented with
Reply 3: It was corrected in the text
Changes in the text: line 138

Comment 4: line 98 measures should be measurements
Reply 4: It was corrected in the text
Changes in the text: line 142

Comment 5: Line 135 - this paragraph does not read well. I would suggest having it in chronological order.
Reply 5: We modified the paragraph according to the suggestion
Changes in the text: lines 180-185