**Dear Dr. Tiago Villanueva**

**Editor-in-Chief, Acta Medica Portuguesa**

**Porto, January 27th 2019**

Thank you very much for your letter on January 16th, with the Reviewer’s comments on our manuscript entitled “A rare case of spontaneous intrauterine skull fracture”. We have accepted and acknowledge the Editor and Reviewer’s suggestions.

Please find below the answers to each of the comments/suggestions:

**Revisor A:**

Relevância:

o manuscrito é importante para a prática clínica de forma geral? Pode ajudar os médicos a aperfeiçoar a sua prática e consequentemente abordar de forma mais eficiente as pessoas com as várias doenças. Comenta factores clínicos, científicos,  sociais, políticos e económicos que afectam a saúde?

Trata-se de um assunto relevante para a prática clínica, nomeadamente por
descrever para a possibilidade da ocorrência de fratura óssea espontânea
em fetos cujas mães têm hipovitaminose D. Nessa sentido, alerta para
evetual necessidade de suplementação de vitamina D em grávidas com
défice (relevância clínica).

Originalidade:

o que é que este manuscrito acrescenta à literatura
existente?

Na verdade, falta um pouco de contextualização relativamente à literatura
existente..

Má conduta:

identifique plágio, imprecisão de dados, fraude, viés e a duplicação de publicação.

Não identificado

Apresentação:

o manuscrito é apresentado de uma forma clara e lógica?

Título:

sumariza bem o manuscrito

Resumo:

faz uma boa descrição do essencial do caso

Discussão:

penso que enriqueceria o trabalho se houvesse uma breve descrição de alguns outros casos, de como foi feito o diagnóstico, bem como qual foi a conduta clínica. No último parágrafo parece-me pouco fundamentado dizer que a combinação dos 3 fatores pode explicar a ocorrência de fratura espontânea do crânico – o torcicolo congénito e a má posição do polo cefálico não parecem ter contribuído para esta fratura, não são assim tão incomuns e não há casos descritos de fratura
espontânea do crânio por esse motivo. Neste caso  a hipovitaminose D é que terá um papel importante.

Recomendação de publicação:

Acha que o manuscrito deve ser publicado na AMP? Porquê? Porque não?

Dado tratar-se de um caso raro teria interesse em ser publicado, após realizadas as alterações sugeridas.

**Resposta ao revisor A**

Comentário 1:

Originalidade: “ Na verdade, falta um pouco de contextualização relativamente à literatura existente”

Resposta:

Os autores aceitam e agradecem a sugestão. De facto, a literatura é bastante escassa, remetendo na sua grande maioria a artigos anteriores ao ano 2000 sem full-text disponível e abordando essencialmente fraturas por depressão ou em “ping-pong”. Do conhecimento dos autores, apenas 2 artigos abordam fraturas do tipo linear, como a do nosso caso, mas que ocorreram após parto vaginal e não cesariana. Nenhum destes artigos faz qualquer alusão a doseamentos de vitamina D ou de cálcio.

Nas alterações realizadas, os autores procuraram ir de encontro às expectativas do revisor e ao mesmo tempo procurando cumprir o número máximo de palavras permitido. De qualquer das formas, encontram-se recetivos a aprofundar mais esta temática, se o revisor considerar pertinente.

De seguida, apresentamos um excerto das alterações executadas no manuscrito:

“The prevalence of spontaneous intrauterine skull fractures varies from 1 in 4000 to 1 in 10000 deliveries. Establishing etiology can be challenging, especially when there is no evidence of abdominal trauma, no use of instruments or after a cesarean section delivery.

There are few similar cases in literature, with the majority of studies describing depressed skull fractures. To our knowledge, this is the first study reporting a linear fracture in a non-traumatic delivery of a newborn with documented hypovitaminosis D. There are no described cases of fractures attributed to vitamin D deficiency, although it has been cited as a cause of congenital rickets and have been associated with suboptimal fetal growth and reduced fetal skull mineralization”.

Comentário 2

“Discussão: penso que enriqueceria o trabalho se houvesse uma breve descrição de alguns outros casos, de como foi feito o diagnóstico, bem como qual foi a conduta clínica. No último parágrafo parece-me pouco fundamentado dizer que a combinação dos 3 fatores pode explicar a ocorrência de fratura espontânea do crânio – o torcicolo congénito e a má posição do polo cefálico não parecem ter contribuído para esta fratura, não são assim tão incomuns e não há casos descritos de fratura espontânea do crânio por esse motivo. Neste caso  a hipovitaminose D é que terá um papel importante.”

Resposta:

Dos 2 casos encontrados que correspondem efetivamente ao mesmo tipo de fratura, 1 deles não foi possível aceder ao full-text para averiguar detalhadamente a conduta clínica e o outro cursou com hemorragia subgaleal que resultou em disfunção multiorgânica e culminou na morte neonatal ao 4º dia de vida. Os autores entenderam que este caso era muito díspar do apresentado e por isso não incluíram uma revisão mais aprofundada da literatura. Os autores reforçam mais uma vez a sua recetividade em realizar mais alterações, se o revisor considerar pertinente.

Quanto ao último parágrafo, foram realizadas alterações de forma a fundamentar a hipótese levantada pelos autores, que se apresentam aqui de seguida. Os autores entendem que, não sendo o torcicolo congénito nem a má orientação do pólo cefálico a causa direta da fratura, estes podem ter sido, num feto já predisposto a fraturas pelo défice de vitamina D e cálcio, um fator adjuvante, na medida em que a má orientação, possivelmente causada pelo torcicolo congénito, poderá ter exposto o crânio fetal a uma maior pressão das estruturas ósseas maternas (coluna lombar, promontório, sínfise púbica, por exemplo). De qualquer das maneiras, não existindo nenhuma descrição prévia na literatura a corroborar isto, os autores procuraram modificar o texto do manuscrito de forma a realçar o caráter hipotético desta teoria.

“Birth trauma has been pointed as the main etiological factor for congenital muscular torticollis (CMT). However, CMT has also been described in cases where no trauma was reported. In our case, congenital muscular torticollis may have been caused by an abnormal intrauterine position during the third trimester which resulted in sternocleidomastoid muscle injury and deformity, as proposed by Stellwagen et al.

The fetal malpresentation, probably due to CMT, may have predisposed the fetus skull to collision with maternal body structures, especially during uterine contractions. The vitamin D deficit and hypocalcemia may have contributed to softening of the fetus skull, predisposing it to fracture.

This is a challenging case in which the combination of three conditions - maternal and fetal hypovitaminosis D, congenital torticollis and malposition of the cephalic pole during labor – may have synergistically contributed to spontaneous intrauterine skull fracture.

**Revisor B:**

• RELEVANCE: This manuscript refers to a very interesting case of
spontaneous skull fracture in a fetus, which the authors believe was caused
by a rare combination of conditions. It is of relevance due to its rarity.

• ORIGINALITY: I did not find a similar case in the literature – The
current version of the manuscript does not highlight the differences between
this case and the ones previously reported and I have suggested for that to
be added to the discussion.

• MISCONDUCT: No evidence of misconduct was apparent.

 STRUCTURE OF THE MANUSCRIPT

•Title: Adequate.

• Abstract: Adequate (although English language can be improved)

• Introduction: Adequate, as it provides a good background reading on the
topic and the potential relevance of this particular case.

• Methods: Not applicable.

• Results: Adequate in general. Suggestions for improvement: a) The
authors argue that a combination of three conditions led to the outcome in
this case. However, they detail one of them (vitamin D insufficiency) while
providing very little information regarding the other two (which is
particularly evident regarding malposition of the fetal head – I added
several questions a comment); b) the presentation of laboratory results
could be improved by the use of a table (with reference values for adults
and newborns).

• Discussion: This is the section with greater room for improvement. The
authors spend most of it discussing vitamin D supplementation in pregnancy,
which is only indirectly related to the case. A separate discussion on each
of the factors contributing to the fracture is strikingly missing. Also
absent is the discussion on how this case compares to others already
published.

• Conclusions: Not applicable.

• References: Most of the references that were used are not free access
(hence I did not always access full text), but they appear adequate. The
style of referencing is inconsistent and only one out of 15 references
complies with AMP style.

• Tables / Figures: Figures are relevant and clear, particularly with the
arrows showed in the main document (I suggested the addition of arrows to
the JPEG files). There are some abbreviations, which should be removed.

• Acknowledgments: Adequate.

EXTENSION:

The manuscript is slightly over the word count limit, while
missing some crucial content in Results and Discussion. I believe the use of
English can be improved to convey more information in less words. Also, the
discussion on vitamin D supplementation in pregnancy appears unnecessarily
long.

PRESENTATION:

The English language is, overall, of a good standard. There
are, however, incomplete sentences and, commonly, incorrect use of articles
– suggestions for improvement have been added as comments. Other than the
Discussion (see above), the content is clearly and logically presented.

**Resposta ao revisor B**

Comment 1

 ORIGINALITY: “I did not find a similar case in the literature – The
current version of the manuscript does not highlight the differences between
this case and the ones previously reported and I have suggested for that to
be added to the discussion.”

Answer:

The authors accept the suggestion. The literature is very sparse on this theme, with most of the articles released before year 2000, without available full-text and reporting depressed fractures or “ping-pong” fractures instead of linear ones. To authors’ knowledge, this is the first study associating spontaneous intrauterine skull fractures with vitamin D deficits or hypocalcemia. The other 2 articles in the literature that report linear fractures happened after a vaginal birth and not cesarean section delivery.

The authors tried to change the discussion according to the reviewer’s suggestion but are receptive to additional changes if the reviewer find appropriate. The alterations are shown below.

Comment 2

• Results: Adequate in general. Suggestions for improvement: a) The
authors argue that a combination of three conditions led to the outcome in
this case. However, they detail one of them (vitamin D insufficiency) while
providing very little information regarding the other two (which is
particularly evident regarding malposition of the fetal head – I added
several questions a comment); b) the presentation of laboratory results
could be improved by the use of a table (with reference values for adults
and newborns).

Answer:

As required, the authors added some additional information about the fetal malpresentation in the results and also a brief explanation in the discussion why the authors believe the other two factors also played a role.

As suggested, a presentation of laboratory results was added to the manuscript.

Comment 3

• Discussion: This is the section with greater room for improvement. The
authors spend most of it discussing vitamin D supplementation in pregnancy,
which is only indirectly related to the case. A separate discussion on each
of the factors contributing to the fracture is strikingly missing. Also
absent is the discussion on how this case compares to others already
published.

Answer:

The authors agree with the reviewer that the discussion should be clarified and that the discussion about vitamin D supplementation was inappropriately long.

The discussion was reviewed, and the alterations are shown below:

“The prevalence of spontaneous intrauterine skull fractures varies from 1 in 4000 to 1 in 10000 deliveries. Establishing etiology can be challenging, especially when there is no evidence of abdominal trauma, no use of instruments or after a cesarean section delivery. There are few similar cases in literature, with the majority of studies describing depressed skull fractures. To our knowledge, this is the first study reporting a linear fracture in a non-traumatic delivery of a newborn with documented hypovitaminosis D. There are no described cases of fractures attributed to vitamin D deficiency, although it has been cited as a cause of congenital rickets and have been associated with suboptimal fetal growth and reduced fetal skull mineralization. ”

(…)

“Birth trauma has been pointed as the main etiological factor for congenital muscular torticollis (CMT). However, CMT has also been described in cases where no trauma was reported. In our case, congenital muscular torticollis may have been caused by an abnormal intrauterine position during the third trimester which resulted in sternocleidomastoid muscle injury and deformity, as proposed by Stellwager *et al.*

The fetal malpresentation, probably due to CMT, may have predisposed the fetus skull to collision with maternal body structures, especially during uterine contractions. The vitamin D deficit and hypocalcemia may have contributed to softening of the fetus skull, predisposing it to fracture.”

Comment 4

• References: Most of the references that were used are not free access
(hence I did not always access full text), but they appear adequate. The
style of referencing is inconsistent and only one out of 15 references
complies with AMP style.

Answer:

The references were corrected in order to comply with AMP style.

Comment 5

Tables / Figures: Figures are relevant and clear, particularly with the
arrows showed in the main document (I suggested the addition of arrows to
the JPEG files). There are some abbreviations, which should be removed.

Answer:

The abbreviations were removed, as suggested. The JPEG files without arrows is a request from Acta Médica Portuguesa.

Comment 6

EXTENSION:

The manuscript is slightly over the word count limit, while
missing some crucial content in Results and Discussion. I believe the use of
English can be improved to convey more information in less words. Also, the
discussion on vitamin D supplementation in pregnancy appears unnecessarily
long

Answer:

The manuscript was reviewed according to reviewers’ suggestions and so that the word limit was fulfilled.

Comment 7

PRESENTATION:

The English language is, overall, of a good standard. There
are, however, incomplete sentences and, commonly, incorrect use of articles
– suggestions for improvement have been added as comments. Other than the
Discussion (see above), the content is clearly and logically presented.

Answer:

The authors were not able to see the suggestions added as comments. Nevertheless, some modifications were made in the manuscript in order to improve the use of articles.