Author's response to reviews

Title: Monozygotic Twins with Neurofibromatosis Type 1, Concordant Phenotype and Synchronous Development of MPNST and Metastasis

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Version: 2 Date: 28 June 2010

Author's response to reviews: see over
June 25, 2010

Dear Editor,

Thank you for the critical review of our manuscript “Monozygotic Twins with Neurofibromatosis Type 1, Concordant Phenotype and Synchronous Development of MPNST and Metastasis.” We have made corrections to the article considering your suggestions:

1. As you suggested, we have shortened the “Case Report” section by summarizing relevant tumoral features of both twins in a paragraph (following suggestions of “Reviewer 2”) and by reporting all other clinical features in a comparative table (table 1) and not then repeating them in full text.

2. Following your suggestion, we have included in the article a critical discussion of current literature about malignant transformation of NF1-associated peripheral nervous tumors. We have based this section on articles proposed by “Reviewer 3,” and other pertinent literature.

3. The original “Bibliography” section was renamed as “References.” After the “References” section a “Competing Interests” section was included. The complete manuscript was send to a professional copyediting service.

4. We are sending you a signed consent to publication of this article from patients, attached to this letter. The document is written in Spanish (as patients are Spanish), and it has a section where the patients directly accepts the publication of their clinical information. If you need a translation, please do not hesitate to contact me. We have confirmed that, in the “Acknowledgements” section, a sentence indicates that we have obtained patients signed consent.

5. Corrections were made considering observations made by your 3 reviewers.
   - **Reviewer 1.**
     a) We have verified that relevant features observed in each twin were compared with previous reports of monozygotic twins with NF1 (“Case Discussion” section). We have also verified that no other reports of NF1 monozygotic twins with MPNST were previously published.
     b) We have sent the manuscript to a professional copyediting service.

   - **Reviewer 2.**
     a) MPNST related features were summarized in a paragraph. All other clinical features are only described in “Table 1.”

   - **Reviewer 3.**
     a) “Reviewer 3” asked us to “confirm that this is in fact the first report of MZ twins with concordant tumors.”
In this article we pretend to explain that, to our knowledge, this is the first reported case of NF1 monozygotic twins with MPNST (we are not considering other type of tumors), in whom the presentation and progression of MPNST was exceptionally similar.

As the manuscript’s paragraph where this argument is considered may not be clear, we have corrected it, in order to express better this idea. As in these days new data about this argument could be published, we have searched again in literature for cases of NF1 twins concordant for MPNST, and we are able to confirm that we could not find any other similar report.

b) We have included in the “Case Discussion” section a critical review of recent articles about current knowledge of molecular changes that may be involved in malignant transformation of NF1 peripheral nervous tumors. We have based this section on articles proposed by “Reviewer 3” and other pertinent literature.

c) Unfortunately, twins’ tumoral samples are not available for further molecular studies.

d) In relation with “Reviewer 3” observation that MPNST concordance, observed in our twins, may be explained by Lubinsky’s theory about vascular fields (Lubinsky 2006), we are agree with this observation, and we have included a paragraph in the “Case Discussion” section, in relation with this topic.

e) We have sent the manuscript to a professional copyediting service.

6. All changes made to the article were highlighted in the manuscript with underlines. Minor changes made by the copyediting service were not highlighted.

Looking forward to hearing from you,

Concepción Hernández Chico
Corresponding author.