Author's response to reviews

Title: The eleventh reported case of Muvihill-Smith syndrome in the literature

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Author's response to reviews: see over
To Editor

Dear Dr.,

Thank you for the attention on our manuscript. As suggested, we have re-written the manuscript in order to improve it. We also thank the referees for their suggestions that really improved the manuscript. We hope the present version can be accepted for publication on this important journal.

With our best wishes,

The authors

To Reviewer 1:

Dear Dr. Caio Imaizumi,
We very much appreciate you for your highly constructive reviews to our submission.

“I don't have questions about this article. I recomend accept this no alterations.”

Answer: We appreciate your time spent and attention on our manuscript.

To Reviewer 2:

Dear Dr. Maria Cristina Digilio,
Thank you very much for your relevant revision on our submission. We have revised the material to eliminate the issues raised. The added or modified words, phrases, and sentences are highlighted in yellow. We hope the present version can be accepted.

“The paper by Breinis et al. is reporting on a new patient with clinical features of Mulvihill-Smith syndrome. The case report is interesting considering the rarity of the syndrome. Nevertheless, it is not adding new information about this condition. Major compulsory revisions
1) The paper is long, particularly the “case presentation” section. This section should be synthesized and schematised, repetitions should be avoided.”

Answer: We really appreciate the kind review on our manuscript. Case presentation section was improved based on the referee’s comments and we also removed repetitions.

“2) Last paragraph of case presentation: the number and location of dental agenesis should be specified”

Answer: We added the following sentence, Case presentation, 5th paragraph:
“Dental agenesis was observed in the second premolar bilaterally and the right maxillary central incisor.”

“3) The degree of mental retardation should be added.”

Answer: We thank the referee for the relevant observation, we included a sentence regarding this matter (Physical examination, 2nd paragraph):

“There was little collaboration with the examiner and a moderate mental retardation and extremely childish behavior.”

“4) The molecular basis of Mulvihill syndrome is unknown, but autosomal recessive mechanism of inheritance is suspected. A sentence should be added to note that the fact that the proband is the only affect child among 8 is not typical for autosomal recessive conditions.”

Answer: This is an important issue raised by the reviewer. We included a sentence in the 1st paragraph of Introduction:

“The Mulvihill-Smith syndrome is a rare and complex genetic disorder, which involves different systems and organs. The description of a patient born to consanguineous parents [9], and the presence of the syndrome in both males and females, leads to a hypothesis of autosomal recessive inheritance. Despite the probable mechanism of its genetic transmission, it is worth noting that this is the only one affected offspring of eight children. The causative gene has not been identified so far [2].”

“5) Which kind of metabolic tests were performed?”

Answer: The metabolic exams performed are added in this new version of the manuscript (Diagnostic investigation, 2nd and 3rd paragraph):

“The metabolic tests performed were total cholesterol and fractions, triglycerides, TSH, T4, serum GH, GOT, GPT, Gamma GT, amylase, blood glucose, blood gas analysis, screening of inborn errors of metabolism blood and urine. Were also analyzed blood count, electrolytes, renal function, ANA, RF, hemoglobin electrophoresis, serology for CMV, Rubella, Toxoplasmosis, Hepatitis B and Epstein Barr, CD3, CD4, CD8, IGF-1 and IGFBP. His blood count revealed lymphocytosis, the dosage of growth hormone and IGF-1 were below the reference value. The CD4 counts were at the lower limit and had a very high parameter of immunoglobulin G to infection with Epstein Barr VCA. All other metabolic tests results were shown normal.”

“6) No mention in the text about genetic examinations. Chromosome analysis and CGHarray should be included.”

Answer: Information on this topic was inserted in the “Diagnostic Investigation” section:
“Clinical evaluation was performed on the genetics sector, and the only test made was the karyotype, which was normal. The hypothesis was diagnosed based on clinical criteria because it is a syndrome with an undefined inheritance.”

“7) The Discussion section should be titled.”

Answer: Discussion section was titled a requested by the reviewer.