

## Revision

42995-Answering Reviewers

REF:

Name of journal: World Journal of Clinical Cases

Manuscript NO.: 42995

Column: Case Report

Title: CONGENITAL ANALBUMINEMIA IN A PATIENT AFFECTED BY  
HYPERCHOLESTEROLEMIA: A CASE REPORT

Authors: Patrizia Suppressa, Concetta Carbonara, Francesca Lugani, Monica Campagnoli,  
Teresa Troiano, Lorenzo Minchiotti and Carlo Sabba'

To: Dr.Fang-Fang Ji

Science Editor, Editorial Office

Baishideng Publishing Group Inc

Dear Dr.Fang-Fang Ji

Many thanks for your kind mail concerning the above mentioned manuscript. We have revised our manuscript according to the reviewers' comments and to the Editor's suggestions listed in the file "Edited Manuscript by Editor". All the raised issues were carefully considered. All the changes made are highlighted in red in the revised manuscript and point-by-point responses to the comments are listed below in this letter.

### **Replies to reviewers**

**Reviewer code:** 03531928

CAA is a rare autosomal recessive disease. There are only dozens of cases in the world. This case report describes detailedly the clinical features and laboratory examinations of a patient with congenital hypoalbuminemia presenting with hypercholesterolemia. More

importantly, ALB gene mutation fragments were detected and analyzed in a patient's family to provide a genetic basis for the diagnosis of the disease. It was also found that the disease did not require albumin infusion, and that atorvastatin was safe and effective in controlling high cholesterol in patients with CCA, helping to reduce their risk of cardiovascular disease. The report is helpful in raising awareness of the disease, providing evidence for genetic diagnosis and related treatment experience, and is recommended for publication.

**Response:** The author wish to thank this referee for his highly positive evaluation of our article and for the appreciation shown towards our work.

**Reviewer code:** 02575809

The article reports a case with a low incidence and with few reports in the literature.

There are abbreviations that should be described the first time they appear in the text. Page 4, homozygous for a CA deletion...

**Response:** homozygous for a CA deletion means that our patient is homozygous for the deletion of two bases, a cytosine and an adenine. The abbreviations for the bases are universally accepted and in our opinion they do not need to be specified.

On page 4 paragraph 3 says... This observation together with the low blood pressure might explain why, despite the high lipid levels, evident clinical signs of early atherosclerosis have not been observed in the patient[3]. In my opinion there are few diagnostic evidence in this patient, or they are not described in the text to say that there are no evident clinical signs of early atherosclerosis.

**Response:** vascular arterial damage was evaluated through ultrasound imaging and no plaques on vessel wall were found. Patient clinical history wasn't suggestive of clinical signs or symptoms of atherosclerosis such as angina, transient ischemic attack, stroke claudication or kidney failure. The absence of other risk factors for atherosclerosis such as high blood pressure, smoking, diabetes, obesity or inflammation diseases might have slowed down this pathological process despite her hypercholesterolemia.

In Discussion he say ... In this case the diagnosis of CCA was not...Review the abbreviation.

**Response:** this was a typographical error. The sentence has been corrected in .... In this case the diagnosis of CAA was not...

... In conclusion, according to our experience, safe and well tolerated hypocholesterolemic treatment with atorvastatin may be administered in dislipidemic patient with CCA should be associated... Review the abbreviation.

**Response:** this was the same typographical error as in the previous point. The sentence has been corrected in .... In conclusion, according to our experience, safe and well tolerated hypocholesterolemic treatment with atorvastatin may be administered in dislipidemic patient with CAA should be associated...

The reference number 8, missing the title of the article

**Response:** reference number 8 was corrected as follows: **Demirsoy E**, Sirin G, Ozker E. Coronary artery bypass surgery in a patient with analbuminemia. *Tex Heart Inst J*. 2011; **38**(1):85-87. [PMID: 21423479 PMCID: PMC3060746].

We wish to thank also this reviewer for his constructive and positive comments and suggestions.

#### **Replies to the points listed in the file “Edited Manuscript by Editor”.**

Comment #1 A short running title of less than 6 words should be provided.

Running title: Hypercholesterolemia in an analbuminemic woman.

Comment #2 Authors' full names should be given first, then the complete name of institution, city, province and postcode.

Authors: Patrizia Suppressa, Concetta Carbonara, Carlo Sabba' (Department of Interdisciplinary Medicine, Geriatric Unit and rare disease Center "A. Moro" University of Bari, 70124 Bari - Italy, Francesca Lugani (Laboratory of molecular Nephrology, Istituto Giannina Gaslini, IRCCS, 16147 Genoa - Italy), Monica Campagnoli, Lorenzo Minchiotti (Department of Molecular Medicine, University of Pavia, 27100 Pavia, Italy) Teresa Troiano (Department of Clinical Pathology, University Hospital of Bari, 70124 Bari - Italy)

Comment #3. Please provide the author contributions. Authors must indicate their specific contributions to the published work. This information will be published as a footnote to the paper. See the format in the attachment file-revision policies.

The paragraph with the author contributions was removed from the final annotations in the previous version and moved where indicated.

Comment #4. Please offer all ORCID number like this: Charles H Halsted (0000-0001-6711-887X); Charles H Halsted (0000-0001-6711-887X).

ORCID number: Patrizia Suppressa (0000-0002-3146-9173), Concetta Carbonara (0000-0001-5301-8050), Lugani Francesca (0000-0002-4189-8561), Campagnoli Monica (0000-0002-0983-6854), Troiano Teresa (0000-0002-6836-5816), Lorenzo Minchiotti (0000-0002-7043-482X), Carlo Sabbà (0000-0002-9874-8740)

Comment #5. Only one corresponding address should be provided. Author names should be given first, then author title, affiliation, the complete name of institution, detail of address (to street or avenue), city, postcode, province, country, and institute email. Thank you!

Correspondence to: Patrizia Suppressa, MD PhD, Department of Interdisciplinary Medicine, Geriatric Unit and rare disease Center "A. Moro" University of Bari, Piazza G. Cesare 11, 70124 Bari, Italy. E-mail:patrizia.suppressa@gmail.com

Comment #6. Telephone and fax should consist of +, country number, district number and telephone or fax number, e.g. Telephone: +86-10-59080039, Fax: +86-10-59080039.

Telephone: +39-080-5592773

Fax: +39- 080-5478126

Comment #7. Signed Informed Consent Form(s) or Document(s). Please upload the primary version (PDF) of the Informed Consent Form (Surgical procedures or other) that has been signed by the patients in the study, prepared in the official language of the authors' country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

The sentence "Informed consent statement: The study participants provided informed written consent prior to their treatments and study enrollment." was removed from the final annotations in the previous version and moved where indicated.

Comment #8. Please offer signed pdf format.

A conflict-of-interest statement is required for all article and study types. In the interests of transparency and helping reviewers to assess any potential bias in a study's design, interpretation of its results or presentation of its scientific/medical content, the BPG requires all authors of each paper to declare any conflicting interests (including but not limited to commercial, personal, political, intellectual, or religious interests) in the title page that are related to the work submitted for consideration of publication. In addition, reviewers are required to indicate any potential conflicting interests they might have related to any particular paper they are asked to review, and a copy of signed statement should be provided to the BPG in PDF format

The sentence:” Conflict-of-interest statement: All authors declare no conflict of interest related to this study or its publication.” was removed from the final annotations in the previous version and moved where indicated.

Comment #9. In order to improve the quality of Case Report manuscripts, authors should download and complete the ‘CARE Checklist (2016) of information to include when writing a case report’ to ensure that the manuscript meets the requirements of the CARE Checklist (2016). Authors must state on the title page of the manuscript that the guidelines of the CARE Checklist (2016) have been adopted (see below). Authors must upload the PDF version of the completed checklist to the system.

CARE Checklist (2016): attached

Comment #10. An informative, structured abstract of no less than 250 words should accompany each manuscript. Abstract should include background, case summary, and conclusion. The Abstract will be structured into the following sections, adhering to the word count thresholds indicated in parentheses:

BACKGROUND (no more than 80 words)

What does this case report add to the medical literature? Why did you write it up?

CASE SUMMARY (no more than 150 words)

What were the chief complaints, diagnoses, interventions, and outcomes?

CONCLUSION (no more than 20 words)

What is the main “take-away” lesson from this case?

In substitution of our previous unstructured abstract, we wrote the following informative, structured abstract:

**BACKGROUND** Congenital analbuminemia is a very rare disorder. Our data describes the clinical features and laboratory results of a new case established by mutation analysis of the albumin gene in a 39-year-old woman presenting with hypercholesterolemia. Our findings contribute to shed light on the molecular genetics of the disorder and confirm that safe and well tolerated hypocholesterolemic treatment with atorvastatin may be administered in dislipidemic patient with congenital analbuminemia in order to reduce their cardiovascular risk.

**CASE SUMMARY** Our patient presented with a history of hypercholesterolemia and referred asthenia and heaviness in both legs. She was born from healthy and non-consanguineous parents and her development was normal. She had not familiarity for early cardiovascular disease, and did not report personal history of hypertension, chronic kidney or liver diseases. Clinical laboratories results showed critically reduced value of albumin whereas other serum proteins were elevated. Main causes of hypoalbuminemia (proteinuria, inflammatory state and insufficient hepatic synthesis) were ruled out by normal procedures and laboratory tests. So the hypothesis of a congenital analbuminemia was tested through mutation analysis of the albumin gene, that revealed a homozygous CA deletion in exon 12, at nucleotide positions c1614-1615. This finding brought to the diagnosis of congenital analbuminemia. Currently the patient receives Atorvastatin 20 mg od and undergoes clinical and laboratory follow-up every six months. She never needed albumin infusions.

**CONCLUSION** Our experience shows how treatment with atorvastatin may be safely administered and well tolerated in patients affected by congenital analbuminemia.

Comment #11. Please offer the audio core tip, the requirement are as follows:

In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications:

**Acceptable file formats:** .mp3, .wav, or .aiff

**Maximum file size:** 10 MB

To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

Audio Core Tip: attached

Comment #12. Under the heading of Case Presentation, the following seven aspects must be presented in this order: 1) Chief complaints; 2) History of present illness; 3) History of past illness; 4) Personal and family history; 5) Physical examination upon admission; 6) Laboratory examinations e.g., routine blood tests, routine urine tests and urinary sediment examination, routine fecal tests and occult blood test, blood biochemistry, immune indexes, and infection indexes; and 7) Imaging examinations e.g., ultrasound, plain abdominal and pelvic CT scan, high-resolution chest CT scan, and head MRI. The patient case presentation should be descriptive, organized chronologically, accurate, salient, and presented in a narrative form.

The suggested scheme is extremely rigid and does not fit well with our case, which is mainly based on laboratory examinations and on molecular biology techniques. We would prefer not to modify our text, which seems to us to be descriptive, organized chronologically, accurate, salient, and presented in a narrative form, exactly as requested. This was confirmed by the positive ratings of the reviewers

Comments #13, 14, and 15. Please write those sections. Thank you.

Final diagnosis: Based on the biochemical findings and on the mutation analysis of the *ALB* the final diagnosis was congenital analbuminemia and hypercholesterolemia, the latter not of genetic origin.

Treatment: Congenital analbuminemia did not require albumin infusions, while hypercholesterolemia was successfully treated with atorvastatin.



Outcome and follow-up: The patient undergoes clinical and laboratory follow-up twice a year. Atorvastatin treatment appears to be successful and well tolerated and so far she never needed albumin infusions.

Comment #16. Please provide the grant approval. Thank you.

The grant approval will be uploaded

Comment #17. Please confirm, is it figure 2?

I confirm that it is figure 2.