June 2nd, 2017

To the Editorial Board of the *"World Journal of Clinical Cases"*

We are submitting our revised manuscript (No: 34458), now entitled: ***"Adrenal Ganglioneuroma: What You Need to Know"*** for your consideration. We would like to thank the reviewers and the Scientific Editor of the Journal, Dr. Fang-Fang Ji, for taking the time and effort to assess our initial manuscript so meticulously. Our research group took into account all of your recommendations and we modified our manuscript accordingly. Detailed replies to the Editor's and the reviewers' comments are provided below:

Replies to the Editor:

Comment 1: *"A short running title of less than 6 words should be provided."*

Authors' reply: Thank you for your guidance. The following short title has been provided: "Adrenal Ganglioneuroma". We also noticed that our initial main title exceed the maximum allowed word count (12 words) and revised it to "Adrenal Ganglioneuroma: What You Need to Know"

Comment 2: *"The order of authors should be consistent with the copyright, please confirm."*

Authors' reply: We apologize for the confusion. The correct order of authors is: Konstantinos S. Mylonas MD, Dimitrios Schizas, MD, PhD, Konstantinos P. Economopoulos MD, PhD. This is depicted in the copyright form as well.

Comments 3-6: *"Please offer the postcode! Thank you!"*

Authors' reply: We apologize for the omission. Postal codes have been added for all institutional affiliations. Also, the title page has been revised to abide by the instructions for authors of the journal.

Comment 7: *"All the authors' work should be given in this section. Thank you!"*

Authors' reply: We apologize for the omission. Authors' contributions have been added as follows: Study design: Mylonas, Economopoulos, Schizas; Collection of data: Mylonas; Drafting of the manuscript: Mylonas; Critical revision of the manuscript for important intellectual content: Mylonas, Schizas, Economopoulos; Supervision: Economopoulos

Comment 8: [Conflict-of-interest statement]:*"Please offer signed pdf file for this statement. 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 it 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!"*

Authors' reply: A signed conflict-of-interest statement has been uploaded along with the revised paper.

Comment 9: [Core tip]: "*Please write a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments. The purpose of the Core Tip is to attract readers' interest for reading the full version of your article and increasing the impact of your article in your field of study."*

Authors' reply: Thank you for your guidance. The following core tip has been added in our revised manuscript (page 3, paragraph 2): "Adrenal ganglioneuromas are uncommon, differentiated tumors which originate from neural crest cells. These lesions are usually discovered incidentally because they tend to be hormonally silent. Even though, surgery is the gold standard for the treatment of adrenal ganglioneuromas, the process of preoperative differential diagnosis remains extremely challenging. Therefore, histologic examination is necessary in order to confirm this rare diagnosis. In general, there is no need for adjuvant treatment and the overall prognosis of these patients is excellent."

Comment 10: [Audio core tip]: "*Please offer the audio core tip, the requirements 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."*

Authors' reply: Thank you for your guidance. An audio core tip has been uploaded along with the revised paper.

Comment 11: *"Please put the reference numbers in square brackets in superscript. Please check across the text."*

Authors' reply: The reference numbers have been placed in superscripted square brackets.

Comment 12: *"Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Pleased provide PubMed citation numbers for the reference list, e.g. PMID and DOI, which can be found at http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed and http://www.crossref.org/SimpleTextQuery/, respectively. The numbers will be used in the E-version of this journal. Thanks very much for your co-operation. Such as: 1 Nayak S, Rath S, Kar BR. Mucous membrane graft for cicatricial ectropion in lamellar ichthyosis: an approach revisited. Ophthal Plast Reconstr Surg 2011: e155-e156 [PMID: 21346670 DOI: 10.1097/IOP.0b013e3182082f4e]."*

Authors' reply: Thank you for your suggestion. PubMed citation numbers and DOI citation have been added to the reference list (which now lists all authors).

Replies to Reviewer #1:

Comment 1.1: *"The paper is well described; the authors should add same further information: - add descriptive information about surgical treatment"*

Authors' reply: Thank you for your thoughtful comment. The following passage has been added in our paper under the heading "MANAGEMENT" (pages 6-7; before the conclusion): "Ultimately, surgery constitutes the gold standard for the treatment of primary adrenal ganglioneuromas. Even though, laparoscopic adrenalectomy is usually the procedure of choice, a number of variables (e.g. hormonal activity, tumor location, and proximity to adjacent structures) also need to be taken into account when deciding on the best approach to operate on these rare tumors. Of note, wide excisions are unnecessary since adrenal ganglioneuromas rarely metastasize or recur. Postoperatively, there is no need for adjuvant therapy in patients with adrenal GNs and their prognosis is excellent."

Comment 1.2: *"…add images of CT or MRI or PET and histopathological features…?"*

Authors' reply: Thank you for your thoughtful suggestions. A number of CT (Figure 1), MRI (Figure 2) and histopathological images (Figure 3) have been added. The Figure Legends are provided after the references (page 11).

Comment 1.3: *"Can the authors add information of GATA-3 marker?"*

Authors' reply: Thank you for your thoughtful suggestion. The following sentence has been added (page 6, paragraph 2): "Additionally, recent case series have found high expression of GATA3 in all of their GN tumors (100%) meaning that this may be a very reliable marker for GNs."

Replies to Reviewer #2:

Comment 2.0: *"This manuscript is interesting, well written and well-summarized. There is a minor comment that should be dealt with before publication. 1. Needs to describe differential diagnosis because of it difficulty of diagnosis and high rate of misdiagnosis."*

Authors' reply: Thank you for your thoughtful suggestion. The following sentence has been added in the second paragraph of page 5: "Taking everything into consideration, preoperative differential diagnosis of GNs remains extremely challenging and includes a variety of lesions, such as ganglioneuroblastoma, neuroblastoma, composite pheochromocytoma, adrenal cortical adenoma and adrenocortical carcinoma."

Replies to Reviewer #3:

Comment 3.0: *"This is an article about the diagnosis, treatment and progress of adrenal ganglioneuromas. The author demonstrate the newly opinion of the disease. It would be much better if the author could provide a few figures of computer tomography, MRI and pathology. Language of the manuscript is fluent."*

Authors' reply: Thank you for your thoughtful suggestions. A number of CT (Figure 1), MRI (Figure 2) and histopathological images (Figure 3) have been added. The Figure Legends are provided after the references.

Last but not least, we carefully reviewed the "Guidelines for Manuscript Preparation and Submission: Minireviews" and subsequently restructured our manuscript to be in line with the expectations of the journal. Particularly, we divide our paper in the following sections: Introduction, Imaging, Histopathologic features, Genetic features, Management, Conclusions. All changes have been highlighted. In conclusion, we hope that with these revisions, our work is felt appropriate to publish in the *World Journal of Clinical Cases* and educational to its readership. We look forward to hearing from you and we would be pleased to answer any further questions and/or comments you may have.

Sincerely yours,

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