Peer Review File

Reviewer Comments

Authors have described the prevalence and ultrasonic patterns of Testicular Adrenal Rest Tumors in Adults with Congenital Adrenal Hyperplasia. The authors concluded that TARTs almost exclusively affected patients with the salt-wasting form of CAH. Furthermore, age at diagnosis and bilateralism were useful factors for achieving a correct diagnosis of TARTs. In general, it's a well-executed study and well-written. I would recommend publication after addressing the following concerns.

REPLY: Dear Reviewer, thank you very much for your encouraging comments. For me and my co-authors this represents a very important opportunity.

1. Title: Suggest to revise as "Prevalence and ultrasonic patterns of Testicular Adrenal Rest Tumors in Adults with Congenital Adrenal Hyperplasia

REPLY: Dear Reviewer, thank you very much for your suggestion. According to it, we modified the title, removing the previous title ("Testicular Adrenal Rest Tumors in Adults with Congenital Adrenal Hyperplasia: Prevalence and Ultrasound Patterns in a Single Center Experience") and introducing the following: "Prevalence and Ultrasound patterns of Testicular Adrenal Rest Tumors in Adults with Congenital Adrenal Hyperplasia".

2. Abstract: Acceptable

REPLY: Dear Reviewer, thank you very much for your encouraging comment.

3. Introduction: This is currently too long. I would suggest to include only the facts relevant to the current study. Extensive description of the clinical features and management of TART is not required.

REPLY: Dear Reviewer, thank you very much for your suggestions. We consequently removed different sentences regarding clinical features and management of TART from the Introduction, as you recommended.

4. Methods: The authors mention that "The CAH diagnosis was performed according to the current guidelines". I would recommend to describe more on the specific diagnostic criteria in detail as this is very relevant to the study.

REPLY: Dear Reviewer, thank you very much for your suggestion. According to your comment, we modified the methods, removing the previous sentence and introducing

the following one: "In all patients, the diagnosis of CAH was made on symptoms and laboratory tests and was confirmed by mutation analysis (33).".

5. I do not understand the 3rd inclusion criteria "the absence of TARTs detected in previous US examinations". This would create substantial bias as those with previously diagnosed TARTS would not be included. To determine the prevalence all adult patients with CAH during the study period should be considered. I would recommend to re-do the analysis after including the patients with a previous diagnosis of TART, at least when reporting the prevalence and also in the ulrasonographic description.
REPLY: Dear Reviewer, thank you very much for punctual observation. We sincerely apologize for this error. Obviously, we agree with you. We removed this sentence from the manuscript. Moreover, in our experience, in the study period all the patients evaluated (>16 ys) were included in the present study population.

6. Authors have performed a multivariate logistic regression analysis which would probably be inaccurate when the sample size is very small as in this study (shown by the large confidence interval). I would suggest to omit it.
REPLY: Dear Reviewer, thank you very much for observation. We agree with you. In fact, due to the limited sample size, the multivariate analysis is affected by an overfitting variables bias. Thus, the results of the multivariate analysis should be interpreted with caution but are still valuable for addressing further larger studies in order to validate our results. According to our suggestion we have now addressed this limit in the discussion section, adding the following sentences in the limitation section: "Furthermore, due to the limited sample size of our study, the multivariate analysis is affected by an overfitting variables bias. However, the results of the present multivariate analysis should be interpreted with caution but are still valuable for addressing further larger studies in order to validate our results.". Finally, we have no problems to remove the multivariate logistic regression analysis if this point became a problem for the positive final decision regarding our manuscript.

7. Results: Authors should report median age with range as the sample size is small, in addition to the mean and standard deviation. Please define the standard deviation in the first instance. Example: "The mean age of this patient population was 25.5 (± 7.26) years" should be "The mean (± standard deviation) age of the patient population was 25.5 (± 7.26) years."
The results and discussion might change if the inclusion criteria is revised.
REPLY: Dear Reviewer, We thank you for the useful advice. Consequently, we have now corrected the text and the tables.

8. Discussion: Well written.

Tables and figures: Acceptable.

REPLY: Dear Reviewer, thank you very much for your positive comments.