Peer Review File

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Review Comments

This manuscript shared a scarce case report of ectopic mediastinal thyroid combined with ectopic parathyroid gland. Both the diagnosis and treatment is challenging due to the lack of definite guidance in the guideline. The favourable prognosis is beneficial to peers. The discussion regarding the potential mechanism is comprehensive and in-depth. However, below are some concerns.

1. Title: The title needs to be changed. It needs to be informative and self-explanatory. What two rare endocrine diseases? Please don't make the author guess whether it's a coincidence or a connection. Focus on the highlights of this study ---the successful diagnosis and treatment.

Thanks to the reviewer for the quality suggestion. We changed the title of the paper, according to the reviewer's suggestions: "Diagnosis and treatment of mediastinal ectopic thyroid tissue with normally located thyroid gland and primary hyperparathyroidism: a case report. See Page 1, lines 1-3.

2. Abstract. Please present the patient's prognosis and follow-up information. Besides, the practical take-home message is required too.

As suggested by reviewer, we added in abstract follow-up information and patient prognosis. In the text: "After surgery, histopathological examination confirmed mediastinal ETT and two PTG adenomas. During follow-up, laboratory analyzes were maintained within the reference range and the patient remained stable and free of symptoms and clinical signs, which supports a good prognosis." See Page 3, lines 9-11.

Also, we added take-home message, as suggested by the reviewer. In the text: "Comprehensive and multidisciplinary surgery planning is a cornerstone of treatment, when recommendations in guidelines are lacking." See Page 3, lines 18-19.
To maintain the number of words in the abstract (below 250), we removed one sentence (30 words) from the text: "We believe this is the first description in the literature until now of ETT with normally located TG (with euthyroid function) and PHPT with eutopic and ectopic adenomas of PTG"(deleted). The abstract now contains 241 words. See Page 3, lines 11-13.

3. Introduction: the introduction is written in a messy way which is not logic. Besides, the unique finding of this case report is not shown by comparing with other related cases.
According to the reviewer's suggestions, we have rewritten certain paragraphs of the introduction (see track changes), with the aim of making it clear and concise. See Page 4, lines 2-23.
Furthermore, we highlighted the uniqueness of our case, as suggested by the reviewer. In the text: "Although similar to the above cases (2-5), we will discuss here the unique case of coexistence of mediastinal ETT and PHPT due to two adenomas, one in an eutopic position on the neck and the other ectopic in the anterior mediastinum positioned adjacent to the ETT." The order of references has been adapted according to the text. See Page 5, lines 6-8.
Thanks for these suggestions. Now the introduction counts 430 words (see track changes), compared to the previous 392 words.

4. Figures: draw a timeline to outline the case as a story that could stand alone.
As suggested, we drew a timeline and tried to present the whole case report in a simple and understandable way ("Timeline of diagnosis, treatment and follow-up for a patient with ectopic thyroid tissue with normally located thyroid gland and primary hyperparathyroidism"). See Figure 6 on Page 19.

5. Figure quality: The resolution of clarity in Figures 1, 2 and 3 need to be improved. In Figures 4 and 5, ABCD is recommended instead of 1234. And, remember to add figure legends for each figure.

We apologize for the poor quality of the previous Figures. Thanks to your suggestion, we have improved the quality of Figures 1, 2 and 3. In Figures 4 and 5, we have replaced the numbers with letters. We have added Figure 6 according to your previous suggestion, and it represents the Timeline of the case report. See Pages 15-19.

6. Discussion: please summarize the major findings from this case report first before any discussion.

We summarized the major findings from the case report before any disscusion, as suggested by the reviewer. In the text: "We have described a unique case of a patient with a combination of ETT in the anterior mediastinum and TG in the anatomical lodge, and PHPT due to two adenomas, one in an eutopic position on the neck and the other ectopic in the anterior mediastinum positioned adjacent to the ETT". See Page 7, lines 20-22.

7. Discussion: use one paragraph to list both strengths and limitations compared to other cases.

As suggested by the reviewer we added paragraph in discussion about limitations and strengths. In the text: "Based on the successful treatment of case and data from literature, we consider clinical examination combined with imaging methods (US, CT scanning and ^{99m}Tc pertechnetate scintigraphy) and CT guided biopsy (in some cases), as the most important steps in the pre-operative diagnosis of ETT. The importance of a broader view on the mediastinal ETT entity in certain circumstances (e.g. in this case coexistence with PHPT) is the main advantage of our case. Consequently, additional diagnostics (US, CT, 99mTc-MIBI parathyroid scintigraphy or choline positron emission tomography [PET]/CT) should be performed, in order to exclude the existence of a hyperfunctional ectopic PTG. The absence of similar cases to date is a major limitation, and a universal diagnostic and surgical approach cannot be defined on the basis of a single case. Consequently, there are no clear recommendations in the guidelines to clarify similar clinical dilemmas. This issue may lead in the future to the possible development of recommendations for additional evaluation of PTG diseases in patients with ETT, with the aim of optimal surgical treatment." See Page 10, lines 11-21.

8. References: please add more cutting-edge references related to the case—for example, ways to diagnose and treat.

As suggested by the reviewer, we added more cutting-edge references related to the case (14-19):

14. Uludag M, Isgor A, Yetkin G, et al. Ectopic mediastinal thyroid tissue: cervical or mediastinum originated?. BMJ Case Rep 2009;2009:bcr09.2008.1004.

15. Walz PC, Iwenofu OH, Essig GF. Ectopic mediastinal goiter successfully managed via cervical approach: case report and review of the literature. Head Neck 2013;35:E94-7.

16. Abdel Aal M, Scheer F, Andresen R. Ectopic mediastinal thyroid tissue with a normally located thyroid gland. Iran J Radiol 2015;12:e7054.

17. Zheng W, Tan J, Liu T. Coexistence of non-functional ectopic thyroid tissue and a normal thyroid: A case report. Exp Ther Med 2013;6:1059-61.

18. Roh E, Hong ES, Ahn HY, et al. A case of mediastinal ectopic thyroid presenting with a paratracheal mass. Korean J Intern Med 2013;28:361-4.

19. Kitada M, Yasuda S, Nana T, et al. Surgical treatment for mediastinal parathyroid adenoma causing primary hyperparathyroidism. J Cardiothorac Surg 2016;11:44.

In the text: "Diagnostic approaches and surgical treatment could be based on the similarities of the described cases (2-4, 14-18). Accordingly, CT (2, 3, 15-17), ^{99m}Tc pertechnetate scintigraphy (3, 14), MR (14) and histological confirmation using CT guided biopsy (15, 16) or EBUS (endobronchial US) - transbronchial needle aspiration (18), were used in the diagnosis of mediastinal ETT. Furthermore, authors have described the transthoracic surgical approach as dominant (2-4), although there is a case of removal of mediastinal ETT through a cervical approach (15). Accurate PTG tissue identification and selection of the optimal surgical method are important. Conventionally, median sternotomy and upper partial sternotomy have been used for surgical excision of mediastinal parathyroid adenomas that are difficult to excise using the cervical approach (19)." See Pages 10, lines 3-10.