

## Peer Review File

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### Reviewer A

**Comment 1:** Introduction and discussion are long and overlapping with same information. Please delete the same information

**Reply 1:** Thank you for your comment.

**Changes in the text:** We deleted the first two paragraphs of the discussion.

**Comment 2:** Please discuss your cases briefly at discussion, especially indications. I see that 2 of your cases had already an indication for surgery (valve and lung cancer). what were the other indications for surgery in your cases.

**Reply 2:** In four patients, there was a concern for malignancy. Patient 1 and 6 had a history of malignancy and there was concern for metastasis. Patient 4 had an anterior mediastinal mass concerning for thymoma. Patient 5 had a heterogeneous and highly vascular mass concerning for paraganglioma or neuroendocrine tumor.

**Changes in the text:** This information was added to the Results > Clinical Presentation section and clarified in the Table.

**Comment 3:** Did you accept them as thymoma and performed a thymoma surgery? How did you decide the extend of resection, did you include thymus? . Please clarify (Why did you resect mediastinal fat ?)

**Reply 3:** Yes, thymectomy was performed for Patient 3 due to the concern for thymoma. The thymus and surrounding pericardial fat were removed.

**Changes in the text:** This information was clarified in the Results > Surgical Resection section.

**Comment 4:** In how many cases you had at least clinical diagnosis?

**Reply 4:** For Patient 1, the surgeon noted a clinical diagnosis of ectopic thyroid, although there was also concern for malignancy

**Changes in the text:** This information was added to the Results > Clinical Presentation section.

**Comment 5:** Please make the presentation concrete and solid to reply the readers' questions?

**Reply 5:** Thank you for your comment.

**Changes in the text:** The manuscript has been reviewed and updated.

### Reviewer B

**Comment 6:** The authors describe their case series of surgical resection of mediastinal ectopic thyroid tissue. I have the following comments:

1)The manuscript is very well written

2)Add the length of stay for the post op course for the patients

**Reply 6:** The mean length of stay was 4.3 days (standard deviation, 1.8 days).

**Changes in the text:** This information was added to the Results > Surgical Resection section.

**Comment 7:** In the figures, reference which patients (from the list in table 1) imaging/pathology is being represented.

**Reply 7:** Thank you for the comment. We have included this information in the figure legends.

**Changes in the text:** For Figures 1-3, the phrase “Preoperative images from Patient #” was inserted at the beginning of the figure legend. For Figure 4, the phrase “Pathologic images from Patient #” was inserted at the beginning of the figure legend.

## Reviewer C

**Comment 8:** I would like to commend Drs Motlaghzadeh, Nesbit, et al., on their study. The main objective of this study was to present a case series of mediastinal ectopic thyroid tissue. They describe the relatively rare occurrence of this subtype of ectopic thyroid tissue, and how this needs to be a consideration in the differential diagnosis of undiagnosed mediastinal masses. The paper evaluated the pathology database at their own institution and found seven cases of mediastinal ectopic thyroid tissue that had been surgically resected between 1996 and 2021. They describe the variable presentation for each other these patients and the variable reasons for need for surgical resection.

This study represents a cases series of resected mediastinal ectopic thyroid tissue in a single institution. The author’s findings demonstrate that there was no discernable pattern to the workup, the radiology findings, or the surgical therapy for any of these resected lesions, and at least two of them were performed as part of a larger operation.

There is a very detailed discussion of the value of different imaging modalities and the ability to obviate the need for surgical resection, however in the case series described, the imaging was mostly either inconclusive for ectopic thyroid, or even if it was consistent with ectopic thyroid the patients had resections for symptoms or for other concurrent disease processes.

There is also mention of the utility of biopsy of the mass for diagnosis or ruling out malignancy, however this was performed in two of the cases and was non-diagnostic in both. The recommendations and the discussion needs to be supported both by the literature review and the review of the cases described in the case series.

**Reply 8:** Thank you for your comments. Unfortunately there are no clear guidelines for management of this rare finding, and few recommendations in the literature.

**Changes in the text:** We added to the discussion, In our retrospective review of seven patients who underwent surgical resection of mediastinal ETT over a 26-year period at our institution, we found some commonalities but many differences. With few recommendations and no guidelines in the literature, we recommend considering this diagnosis for a mediastinal mass and careful preoperative evaluation before surgical resection.

**Comment 9:** A more concrete takeaway from undertaking this case series review is needed for the manuscript. The conclusion that the disease process is rare and should be managed on an individualized basis, while is likely to be true, does not substantially move forward the collective knowledge of the disease process.

Overall, I enjoyed reading this well written article, and I would like to thank the authors for their manuscript and contribution to the treatment of this very rare disease process.

**Reply 9:** Thank you for your comment. We were hoping to find a higher number of cases from which more substantial conclusions could be drawn. However, with a small number, we can only recommend considering ectopic thyroid when evaluating mediastinal masses. And after collaborating with endocrinologists on this project, checking thyroid function before and after surgery.

**Changes in the text:** We edited the Discussion as per the previous comment.

## **Reviewer D**

**Comment 10:** Interesting cases on this rare entity. However, more information is needed for some cases and there are some discrepancies.

Patients under 18 years of age and those with metastatic thyroid cancer to the mediastinum were excluded.” Do the patients have thyroid physical or imaging examination? Thyroid fine-needle aspiration or biopsy and pathologic evaluation of thyroid?

**Reply 10:** Thank you for your comment. We excluded patients with a known history of thyroid neoplasm, but did not document the initial evaluation of the thyroid. In reviewing the data to respond to your comment, we did note that Patient 2 underwent mediastinoscopy and Patient 6 underwent endobronchial ultrasound (EBUS) guided biopsy which were both nondiagnostic.

**Changes in the text:** This information was clarified in the Methods section and added to the Results > Clinical Presentation sections.

**Comment 11:** Discrepancies: “Before surgery, the diagnosis of ectopic thyroid tissue was probable in all patients, but no one had a biopsy proven diagnosis”. But in Radiology, you mentioned “Patient 3 underwent ultrasonography of the neck which showed a 1.9 cm solid isoechoic noncalcified right thyroid nodule which was found to be benign on FNA biopsy.” In discussion, it said “Two of our cases also underwent biopsy of the mediastinal masses.”

**Reply 11:** Thank you for your comment. This biopsy was for a thyroid nodule in the neck, not the mediastinal mass.

**Changes in the text:** This information was deleted from the Results > Radiology section.

**Comment 12:** There were no features of malignancy: explain in detail?

**Reply 12:** Thank you for the question. Our pathologist explained, no features of classic papillary thyroid carcinoma, including enlarged pale nuclei, irregular nuclear contours, longitudinal nuclear grooves, intranuclear pseudoinclusions, or dense squamous cytoplasm are seen. No marked cytologic atypia, elevated mitotic activity, or necrosis is seen.

**Changes in the text:** This information was added to the Results > Pathology and Figure 4

legend.

**Comment 13:** There are some discrepancies between Table 1 and Case Presentation, such as “Three of the patients had thyroid stimulating hormone (TSH) check before and after surgery and one patient after surgery.” But in the table, 2 had thyroid stimulating hormone (TSH) check before and after surgery, 1 had before surgery and 1 had after surgery.

**Reply 13:** Thank you for pointing out this discrepancy.

**Changes in the text:** The text in Results > Clinical Presentation has been corrected.

**Comment 14:** “Patient 3 underwent ultrasonography of the neck which showed a 1.9 cm solid isoechoic noncalcified right thyroid nodule, in the table it said “2.7 cm”, etc.

**Reply 14:** The thyroid nodule was 1.9cm, while the mediastinal mass was 2.7cm.

**Changes in the text:** We deleted the information about the thyroid nodule biopsy, since this was not relevant to the mediastinal mass.

**Comment 15:** One of the patients who had a robot-assisted approach had a combined lobectomy for concern of malignancy. What is the pathologic diagnosis after the surgery for both?

**Reply 15:** The lung lobectomy was performed for neuroendocrine tumor.

**Changes in the text:** This information was added to the Results > Surgical Resection section.

**Comment 16:** In Figures, check the arrow position and there are no arrows in some Panels.

**Reply 16:** The arrow positions have been confirmed. A \* was added to Figure 3C,F to mark the thyroid.

**Changes in the text:** Figure 3C,F and Figure 3 legend were updated.

**Comment 17:** In discussion, “One of the limitations of the study is that we reviewed pathology database, so we do not have a comparison group for non-surgical patients.” In our experience, the cases of nonsurgical patients are in the cytology database. Cytology database reviewed?

**Reply 17:** The cytology database was reviewed as part of the pathology database, and there were no nonsurgical patients identified.

**Changes in the text:** None.

**Comment 18:** Please check typographic errors.

**Reply 18:** Thank you for your comment.

**Changes in the text:** The manuscript has been reviewed and edited.