Peer Review File

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Reviewer A

Comment 1: This case describes an important aspect of remote-access thyroidectomy clearly and is well-illustrated with images. I only have minor comments.

Reply 1: We sincerely appreciate the reviewer's time and effort in evaluating our manuscript. We have revised the text in accordance with your helpful and constructive comments, which have enabled us to improve the manuscript.

Comment 2: In line 111, the size of 4,1 cm seems very large, is this the sum of all tumor foci removed, or was there one single tumor that large? Is it possible to estimate how many separate foci that were removed?

Reply 2: The reported size of 4.1 cm represents the cumulative measurement of all tumor foci that were removed. We have further clarified this point in our manuscript. Due to the numerous pieces and the complexity of the specimen, it was challenging to accurately estimate the exact number of separate foci removed.

Changes in the text: (Lines 110-111) Histopathology confirmed metastatic follicular thyroid carcinoma in the soft tissues in the lower lip, strap muscles, and neck levels I, IIA, and VI, with a combined measurement of all tumor foci up to 4.1 cm in greatest diameter.

Comment 3: Line 291-93 and 302-307 Figure legends 1 and 3: several words are divided between lines

Reply 3: We appreciate your observation. However, it appears that the word division issue in the Figure legends section occurred on the journal submission site and is not within our control.

Comment 4: Line 148: The risk of malignancy in Bethesda III or IV is higher than the estimates suggested, see updated numbers in the Bethesda 2023 classification doi: 10.1089/thy.2023.0141.

Reply 4: Thank you for your valuable comment. We would like to clarify that our reference was to nodules with benign preoperative cytology results. To address this, we have made appropriate modifications for clarity. Additionally, we have updated the manuscript to accurately represent the risk of malignancy in Bethesda II (benign) categories, incorporating the relevant information from the Bethesda 2023 classification, as recommended by the reviewer.

Changes in the text: (Lines 149-151) The risk of malignancy for benign cytology results can range from 2% to 7%, particularly in cases where the nodule is larger in size (21, 22).

Changes in the text: (Lines 277-278: References) 22. Ali SZ, Baloch ZW, Cochand-Priollet B, Schmitt FC, Vielh P, VanderLaan PA. The 2023 Bethesda System for reporting thyroid cytopathology. J Am Soc Cytopathol. 2023;12(5):319-25.

Comment 5: Line 174: It would be good to know if distilled water was used in the current case. A common precaution in similar cases is to put the specimen in a plastic bag before extraction. This should be mentioned as a possible precaution/implication.

Reply 5: In response to your comment on Line 174 regarding the use of distilled water, we

confirm that, as stated in Line 93, we exclusively suctioned the visible thyroid tissues without utilizing distilled water. To enhance clarity, we have explicitly mentioned in our manuscript that distilled water was not employed. Furthermore, we placed the main. specimen into a plastic specimen bag before extraction through the middle port as shown in Line 94. We added "plastic specimen bag" for clearer description. As for the precaution of putting the specimen in a specimen bag before extraction, we have already discussed it in lines 166-167 ("Using a specimen bag to retrieve the resected specimen is a common preventative measure to minimize iatrogenic implantation,".

Changes in the text: (Line 93) all visible thyroid tissue was meticulously suctioned without distilled water irrigation.

Changes in the text: (Line 94) inserted into a plastic specimen bag

Changes in the text: (Line 180) inserted into a plastic specimen bag

Reviewer B

Comment 1: The authors honestly reported a rare but major adverse event of transoral thyroid lobectomy done for a thyroid nodule with inconclusive preoperative cytology result: follicular lesion of undetermined significance.

Reply 1: We sincerely appreciate the reviewer's time and effort in evaluating our manuscript.

Comment 2: The nodule is 4cm with capsule breaching during endoscopic dissection, resulting in seeding recurrence. What is the upper limit of thyroid nodule dimension, in general, suitable for safe transoral endoscopic thyroidectomy? Will conversion to open thyroidectomy for this case be advisable to preclude seeding recurrence for better lavage of microscopic tumor cell spillage & meticulous removal of R thyroid lobe. (Fig. 2A displays substantial right thyroid remnant left behind along with recurrent tumor.)

Reply 2: Thank you for raising an important point. As of now, there is no established guideline specifying the upper limit of thyroid nodule size for safe consideration of TOETVA. Generally, TOETVA is indicated for benign diseases, and a suggested upper limit for thyroid tumor size is often considered to be <6cm, with some surgeons recommending nodules <4cm. In this particular case, despite the relatively large size of the nodule (almost 4 cm), we opted for TOETVA based on the benign preoperative gun biopsy results, the patient's age, and the patient's preference for this procedure. To provide clarity on the indications for TOETVA, we have included relevant information in our manuscript. We appreciate your insightful comment and trust that this clarification enhances the understanding of our decision-making process.

As for the comment on conversion to open surgery, in retrospect, it would have been prudent to contemplate transitioning to an open thyroidectomy for the thorough elimination of microscopic tumor cells and the entire right thyroid lobe. Regrettably, we failed to recognize that even in cases of a benign tumor, there exists the potential for recurrence through seeding. Therefore, we have added the comment that emphasizes the necessity of considering open conversion when there is tumor spillage or an inability to retrieve it completely, even in the case of a benign preoperative diagnosis.

Changes in the text: (Lines 159-166) Currently, there is no established guideline specifying the upper limit of thyroid nodule size for safe consideration of TOETVA. Generally, TOETVA is indicated for benign diseases, papillary microcarcinoma, and thyroid nodules smaller than 6

cm,(26) with some surgeons suggesting a threshold of less than 4 cm.(4) In this particular case, despite the relatively large size of the nodule, almost 4 cm, we chose TOETVA based on the benign preoperative biopsy results, the patient's age, and the patient's preference for this procedure. Although a large nodule size may not be a contraindication for TOETVA, surgeon judgment and expertise are crucial when dealing with larger nodule sizes.

Changes in the text: (Lines 184-186) Moreover, surgeons should also consider converting to an open approach in situations involving tumor spillage or an inability to fully retrieve it, even when dealing with a benign preoperative diagnosis.

Changes in the text: (Lines 287-289: References) 26. Anuwong A, Sasanakietkul T, Jitpratoom P, Ketwong K, Kim HY, Dionigi G, et al. Transoral endoscopic thyroidectomy vestibular approach (TOETVA): indications, techniques and results. Surg Endosc. 2018;32(1):456-65.

Comment 3: This rare complication should be included in the complications of endoscopic thyroidectomy when obtaining informed consent before operation. Please emphasize this point in Discussion.

Reply 3: Thank you for your valuable feedback. We recognize the significance of including this rare complication in the list of potential complications discussed during the informed consent process for endoscopic thyroidectomy. In line with your suggestion, we have highlighted this point in the discussion section of our manuscript to underscore its importance in the overall context of surgical considerations.

Changes in the text: (Lines 200-202) Surgeons need to be conscious of this atypical complication and it should be addressed as a potential complication of TOETVA when obtaining informed consent before operation. Surgeons must be prepared to counsel patients appropriately, including the recommendation of medical strategies

Comment 4: A low collar incision was employed for completion thyroidectomy, central node dissection & removal of recurrent tumour in the lower neck in June 2022. A 2nd operation via a submental incision was carried out 2 weeks later to clear the upper neck & chin recurrences. Why was a 2-stage operation planned & conducted, instead of 1, to salvage the seeding recurrence spanning from submental area to thyroid bed?

Reply 4: Thank you for your insightful comment. Originally, our intention was to perform the required procedures in a single operation, utilizing a low collar incision and a small incision in the lower lip. However, during the initial surgery, it became apparent that accessing the upper neck and chin recurrences through these incisions was challenging. Consequently, following the first operation, we conducted a CT scan to precisely identify the location of remaining recurrences, prompting the need for a second surgery. The submental incision was chosen strategically to directly address and resect the identified remnant recurrences in the upper neck and chin areas. This two-stage approach was implemented to ensure thorough and effective salvage of the seeding recurrence spanning from the submental area to the thyroid bed. We have added this explanation in our manuscript for clarification.

Changes in the text: (Lines 115-118) Due to the challenges encountered in accessing the upper neck and chin recurrences through the incisions, a neck CT scan was conducted on the second postoperative day. The scan aimed to assess the extent of remaining nodules, revealing their presence in the subcutaneous tissue of the upper neck and chin, prompting consideration for a

second-look operation.

Reviewer C

Comment 1: The case is interesting and unusual, describing a problem after a new technique.
Reply 1: We thank the reviewer for showing interest in our case report. We sincerely appreciate the reviewer's time and effort in evaluating our manuscript.

Comment 2: Criteria for selection of patients for TOETVA have to be discussed.
Reply 2: Thank you for raising an important point. To provide clarity on the indications for TOETVA, we have included relevant information in our manuscript.
Changes in the text: (Lines 159-166) Currently, there is no established guideline specifying the upper limit of thyroid nodule size for safe consideration of TOETVA. Generally, TOETVA is indicated for benign diseases, papillary microcarcinoma, and thyroid nodules smaller than 6 cm,(26) with some surgeons suggesting a threshold of less than 4 cm.(4) In this particular case, despite the relatively large size of the nodule, almost 4 cm, we chose TOETVA based on the benign preoperative biopsy results, the patient's age, and the patient's preference for this procedure. Although a large nodule size may not be a contraindication for TOETVA, surgeon judgment and expertise are crucial when dealing with larger nodule sizes.
Changes in the text: (Lines 290-292: References) 26. Anuwong A, Sasanakietkul T, Jitpratoom P, Ketwong K, Kim HY, Dionigi G, et al. Transoral endoscopic thyroidectomy vestibular approach (TOETVA): indications, techniques and results. Surg Endosc. 2018;32(1):456-65.

Comment 3: Photos are good
Reply 3: Thank you for the valuable feedback. We meticulously selected photos that precisely illustrate our case. Your encouragement inspires us to continue our commitment to thorough reporting and sharing of our clinical experiences.

Reviewer D

Comment 1: The case report is very well written and highlights the importance of using the right approach for indeterminate or suspicious cytology to avoid such complications.
Reply 1: Thank you for the encouraging comment. We sincerely appreciate the reviewer's time and effort in evaluating our manuscript.

Comment 2: What was the TIRADS score for the lesion?
Reply 2: We appreciate your attention to detail. The TIRADS score for the initial lesion was 3. While this information was included in the figure legend, we acknowledge that it was inadvertently omitted from the manuscript. We have now rectified this oversight by incorporating the TIRADS score information into the manuscript to ensure comprehensive and accurate reporting. Thank you for bringing this to our attention, and we believe this addition strengthens the clarity of our findings.
Changes in the text: (Lines 85-86) Ultrasonography (USG) revealed a Thyroid Imaging Reporting and Data System 3 isoechoic solid nodule without marked vascularity, measuring 2.8 cm in the right lower thyroid.

Comment 3: Especially would be useful to know the vascularity of the lesion. If the lesion was very vascular with suspicion for atypia, the surgeon may have considered an open approach.
Reply 3: We appreciate your attention to detail. There were no signs of marked vascularity on doppler sonography, and we have added this description in our manuscript, as the reviewer suggested. Thank you once again for your time, feedback, and support. We look forward to further enhancing the manuscript based on your suggestions.
Changes in the text: (Lines 85-86) Ultrasonography (USG) revealed a Thyroid Imaging Reporting and Data System 3 isoechoic solid nodule without marked vascularity, measuring 2.8 cm in the right lower thyroid.

Reviewer E

Comment 1: The authors describe the first known case of seeding recurrence of follicular thyroid carcinoma following TOETVA thyroid lobectomy for a 4cm thyroid nodule that was initially benign of preoperative biopsy. Intraoperative rupture of the tumor occurred. Pathology showed a 3.0cm follicular thyroid carcinoma and a papillary microcarcinoma. Recurrence was noted on postoperative surveillance and salvage was attained with two operations and two doses of radioactive iodine with no subsequent structural or biochemical evidence of disease.
It is vitally important to publish these cases and findings as a newer technology/approach is being more widely implemented. I commend the authors on their management and transparency and recommend this important case be published as it highlights the importance of long-term surveillance for structural recurrence as well as the point of tumor rupture predisposing to seeding and recurrence.
Reply 1: We sincerely appreciate your thoughtful review and commendation of our work. Your recognition of the importance of publishing this case, particularly in the context of the increasing implementation of newer technologies and approaches like TOETVA, is invaluable. We share your commitment to transparency and believe that sharing such cases contributes significantly to the collective understanding of potential complications and long-term considerations. Thank you once again for your time, feedback, and support. We look forward to further enhancing the manuscript based on your suggestions.

Comment 2: As a point of clarification, in lines 107-111 where describing the reoperation, it is described that a low collar incision was used, but the pathology described lower lip disease - how was the lower lip recurrence addressed?
Reply 2: We appreciate your insightful comment, and we acknowledge that we have omitted the information regarding the management of lower lip recurrence. The lower lip recurrence was addressed by utilizing an incision in the lower lip, similar to the middle port incision made during TOETVA. To provide clarity on this matter, we have included this information in our manuscript. Thank you for bringing this to our attention, and we trust that this clarification enhances the understanding of our surgical approach in managing the lower lip recurrence. Additionally, we have included the CT scan images of the lower lip in Figures 2 and 4,
Changes in the text: (Line 110) performed through a new low-collar incision on the neck and a small incision in the lower lip.
Changes in the text: (Line 315: Figures legend) (C) at right chin subcutaneous layer (yellow arrow), and (D) at the lower lip subcutaneous layer (red arrow).

Changes in the text: (Line 325: Figures legend) (C) chin, and (D) lower lip subcutaneous layer.