

Peer Review File

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Reviewer A

Major revisions

1. The authors should provide a descriptive history of the patient's thyrotoxicosis before this admission. For example, how long has she had a diagnosis of Graves's disease, how long has she received the antithyroid medication, her thyroid function tests, and her compliance?

Reply: We thank Reviewer A for taking the time to review our manuscript and for their comments. Unfortunately, the patient was followed and treated in another country prior to admission, and we were unable to obtain her medical records. She presented to our institution due to worsening symptoms with lack of medication compliance. We elaborated upon the time prior to her presentation.

Changes in the text: Added lines 146-150.

2. According to line 147, the patient reported the significant compressive symptom accelerated within a month. Without acute complication, Graves' disease and toxic MNG patients usually present with gradually worsening symptoms for more than 3 months. Authors should provide more details to clarify the possible cause of these rapid deterioration?

Reply: The trigger was most likely her medication noncompliance.

Changes in the text: Added to lines 151-153.

3. The author should provide a timeline presenting major clinical changes, TFT, and treatments.

Reply: The Case Presentation section was written in a chronological order, including all of the patient's clinical changes, exam results, and treatments.

Changes in the text: none.

4. According to line 155, the patient underwent CT scan to evaluate her thyroid mass. Authors should declare that CT scan was performed with or without contrast injection because iodine from intravenous contrast can worsen her thyrotoxicosis.

Reply: This point is very important since, as stated by the reviewer, iodine contrast can worsen the patient's thyrotoxicosis.

Changes in the text: We added to line 161-162 to indicate the absence of iodine contrast use in the CT imaging.

5. The authors should provide the TFT at the FNA date and before thyroidectomy, if available because the patient received antithyroid treatment a couple of days before.

Reply: We have T3, T4, and TSH levels at admission and one day post-FNA available. We had reported the pre-FNA values at admission in lines 157-159 but agree the post-FNA levels should be added to the manuscript.

Changes in the text: Added line 184-185.

6. The authors should show the thyroid storm criteria regarding Japan Thyroid Association Akamizu's 2016 due to the higher specificity than BWS.

Reply: We agree that the Japan Thyroid Association criteria are important to utilize in our case report.

Changes in the text: We have added lines 181-183 to the manuscript.

7. After the acute management in ICU, her FT4 and TT3 successfully decreased to the normal range (line 179). May the thyrotoxicosis not be the primary cause of clinical deterioration? Was the goiter's compression the primary cause? So, she improved after the total thyroidectomy.

Reply: Her goiter and compressive symptoms played a role in her sick status. However, her clinical deterioration occurred right after she had the FNA procedure, developing a thyroid storm. Her free T4 was trending down, however it still was 2 times the upper limit of normal.

Changes in the text: None.

8. Some articles studying the Doppler flow in thyroid ultrasound can screen the hyperfunctioning thyroid nodules if patients cannot perform a thyroid scan or uptake. Authors should discuss this point in the investigation for assessing hyperfunctioning thyroid nodules.

Reply: This point adds to our focus in the third paragraph of our Discussion and is useful information for readers.

Changes in the text: We have added lines 234-236 to the manuscript accordingly.

9. According to line 268, the author should provide the appropriate supporting scientific evidence and mechanism of " ... suggesting beta blocker stop thyroid hormone release during thyroid gland manipulation." Beta blockers, especially high dose propranolol, are well-known to decrease thyroid hormone conversion at peripheral tissue, not directly inhibit the thyroid gland.

Reply: In the manuscript, we did not indicate that beta-blockers directly inhibit the thyroid gland, as they do not. We further elaborated upon their inhibition and effects as suggested by this reviewer.

Changes in the text: Added lines 285-287.

Minor revisions

1. According to line 140, "...to create awareness that complication like thyrotoxicosis can happen..." Did the authors mean thyroid storm because the patient was already diagnosed thyrotoxicosis before FNA?

Reply: Yes, it should have read as "thyroid storm" rather than "thyrotoxicosis." This error has been corrected in the manuscript.

Changes in the text: Line 140 was updated accordingly.

2. The authors should provide the normal range of thyroid-stimulating immunoglobulin (TSI) and TSH receptor antibody (TRAb).

Reply: Normal ranges should always be indicated. We did so in parentheses for other values but failed to for TSI and TRAb.

Changes in the text: Lines 160-161 have been updated to include these normal values.

3. The authors should provide all the essential in-admission laboratory parameters in the table with normal values.

Reply: These values were presented in the manuscript, however, as stated above, we failed to for TSI and TRAb.

Changes in the text: Lines 160-161 have been updated to include these normal values.

4. Thyroid ultrasound should be described and classify risk of each nodule according to ATA thyroid imaging guidelines.

Reply: We agree and have added the thyroid ultrasound results according to ATA imaging guidelines.

Changes in the text: Added lines 167-171.

5. According to line 171, the patient developed altered mental status and signs of airway obstruction. The non-invasive ventilation is contraindicated regarding the inability of airway protection.

Reply: The reviewer is correct in their assertions. However, she was placed on NIV for a few hours per decision of the ICU team and intubated thereafter to protect her airway.

Changes in the text: Clarified this chain of events and contraindication in lines 185-188.

Reviewer B

In this report, authors presented a case of 62-year-old female patient with history of multinodular goiter (MNG) disease who experienced a thyroid storm after she underwent a fine needle biopsy

(FNB) and the subsequent emergent treatment with a total thyroidectomy. Thyroid FNA is a procedure of simplicity, accuracy and cost-effectiveness and routinely used as an initial diagnostic approach in the management of thyroid nodules. However, there are potential complications following diagnostic thyroid FNB under certain settings, which have not been reported in the literature yet or existing data are insufficient to support them. This report describes a case with conditions that FNA biopsy should be used with caution, complications that the thyroid FNB triggered, and management measures that were taken. It is clinically important to be aware of conditions, subsequent complications and treatment options before attempting to perform an FNA. The report is well written and conveys a key clinical message.

The reviewer has one concern.

Specify that this report has been presented in previous meetings. (It was published in Journal of the Endocrine Society, Volume 6, Issue Supplement_1, November-December 2022, Pages A829–A830.)

Reply: We thank Reviewer B for taking the time to review our manuscript and for their comments. The abstract and poster for this case report was presented and published by the Journal of the Endocrine Society Conference. It was thereafter expanded into this manuscript, which has not been published elsewhere.

Changes in the text: We added this point to the disclosures.

Reviewer C

This is a well-written manuscript about a case of a thyrotoxic storm secondary to FNA biopsy. It is very important to check the thyroid status for patients undergoing thyroid biopsy as it should be avoided in a hyperthyroid state.

Few comments:

Make sure to change betablockers to beta-blocker to be consistent throughout the manuscript

Reply: We thank Reviewer C for taking the time to review our manuscript and for their comments. Spelling/hyphens should be consistent throughout the manuscript. We updated accordingly.

Changes in the text: All versions of this term were changed consistently to “beta-blockers” throughout the manuscript.

Consider removing the first sentence in the discussion, line 203 “Patients with active hyperthyroidism should not undergo biopsy.” as it does not look good at the start of the discussion section and it is already mentioned later in the discussion.

Reply: We concur that this is repetitive and inappropriate to begin the Discussion section with.

Changes in the text: The sentence in line 203 to which Reviewer C refers has been deleted from the manuscript.

Please remove the sentence in line 249 “It is important to have full support in the ICU.”

Reply: We agree this sentence is unnecessary.

Changes in the text: The sentence in line 249 to which Reviewer C refers has been deleted from the manuscript.

Reviewer D

This paper regarding thyroid storm after FNA in the setting of Graves disease is clinically relevant and in an important entity about which to raise awareness. This was well written, and I have just a few minor recommendations as below.

Change "Graves'" and "Grave's" to "Graves" throughout as it is named after Dr. Robert Graves who discovered it.

Reply: We thank Reviewer D for taking the time to review our manuscript and for their comments. While Graves’ disease is named after Dr. Robert James Graves, the apostrophe after the s in his name is necessary as it indicates Dr. Graves’ possession of the disease and is included in the formal title of the disease.

Changes in the text: none.

Line 170 remove "about"

Reply: We agree that “about” does not belong in this sentence.

Changes in the text: “About” in line 170 to which Reviewer D refers has been removed from the manuscript.

Line 257 change to "patients with Graves disease"

Reply: Reviewer D’s rewording of our sentence reads much more eloquently.

Changes in the text: We have updated line 273 accordingly.