

Peer Review File

Article Information: Available at <http://dx.doi.org/10.21037/aot-20-57>

Reviewer A

Comment 1: What gauge needle was used? How many passes were performed? Were there any immediate complications from the FNAB?

Reply 1: The gauge of the needle used and the number of passes performed were not documented by the radiologist who performed the FNAB. It was however documented that there were no immediate complications after the procedure.

Changes in the text: we have included the text “no immediate complications after the procedure” (see page 4, line 49)

Comment 2: How soon after aspiration did these symptoms develop?

Reply 2: She developed hoarseness of voice about 11 days after the procedure.

Changes in the text: We have modified our text to include the approximate onset of symptoms (see page 4, line 53)

Comment 3: were previous liver tests available?

Reply 3: She had no previous liver tests or prior history of liver disease.

Changes in text: We have modified our text as advised (see page 5, line 64)

Comment 4: what investigations for infection were performed?

Reply 4: chest x-ray to exclude pneumonia, abdominal ultrasound to exclude biliary sepsis, repeat thyroid ultrasound to exclude suppurative thyroiditis/thyroid abscess and blood cultures.

Changes in text: We have modified our text to specify chest x ray (see page 5, line 74). The rest of the investigations are mentioned elsewhere in the manuscript (abdominal ultrasound, repeat thyroid ultrasound)

Comment 5: please provide reference ranges for liver related tests.

Reply 5: ALT (11 – 55 u/L), ALP (30 – 130 u/L), Bilirubin (0 – 21 umol/L)

Changes in text: We have modified the table to reflect the reference ranges. (see table 1)

Comment 6: It is noted that the thyroid and liver tests were starting to improve before steroids were given (based on table). How can the authors be sure that the steroids improved her symptoms, and not that her symptoms would have improved on their own without treatment? The authors acknowledge that prior cases seemed to have the same trajectory whether steroids were used or not.

Reply 6: There were marked improvement in the free T4 (at least 15 %), ALT (~ 38%) and CRP (~60%) on the 3rd day following steroid therapy. Clinically, the fever ceased the next day after administration of steroids and she felt reduced pressure in the neck. The rapid improvement in her symptoms provided further assurance for her to be safely discharged from hospital. The decision to

treat with steroids was not purely due to biochemical derangement but due to clinical symptoms (pressure in the neck, hoarseness, fever, tachycardia). The number of cases from the previous study is too small to reach any definite conclusion. The

Changes in text: We have modified our text to justify the use of corticosteroids (see Page 6, line 89; Page 7, line 142)

Reviewer B

Comments 1: Authors describe a cause of thyrotoxicosis in this case is FNAB. I understand that clinical course of this case reminiscent of it, however, it is insufficient differentiation from other causes of thyrotoxicosis. Is there a possibility of thyrotoxicosis due to acute suppurative thyroiditis or subacute thyroiditis? How to exclude these diseases?

Reply 1: We did exclude other causes of thyrotoxicosis. We excluded acute suppurative thyroiditis on clinical grounds and performed a repeat ultrasound of the thyroid to exclude an abscess. Thyroid receptor antibody (TRAB) was normal thereby excluding Grave's thyrotoxicosis.

Changes in text: We have added the text to reflect that Grave's thyrotoxicosis was excluded (see Page 5, line 79)

Comments 2: As authors described, the mechanism by which post-aspiration thyrotoxicosis occurs is still debated. From this point of view, Authors should describe in more detail the needle size, pre-treatment before FNAB.

Reply 2: The size of the needle used for the FNAB was not documented by the radiologist who performed the procedure and there was no pretreatment with steroids, Lugol's iodine or any other medication prior to the procedure. In the prospective study by Kobayashi et al, they found that the post-aspiration thyrotoxicosis was unrelated to the size of the gauge of the needle.

Changes in text: we have included the text "no immediate complications after the procedure" (see page 4, line 49)

Comments 3: Is this the first time FNAB has been performed in this case? Can thyroiditis develop repeatedly with each FNAB? Please clarify whether this patient have a history of aspiration in the past.

Reply 3: No, it is not the first time FNAB has been performed in this case. She had initial aspiration on 21/07/2014 and the histology was indeterminate (Thy 3a) and a repeat aspiration was performed on 30/07/2014 and the histology showed colloid nodule (Thy 2). Unfortunately, thyroid function test was not done following the procedure on both occasions. From previous case studies, the incidence of biochemical thyrotoxicosis is probably higher if thyroid function test is monitored before and after FNAB. It appears that the FNAB done in 2014 was for diagnostic purpose and therefore focussed on the nodular component whereas the incident case focussed on therapeutic and aspiration of the cystic component.

Changes in text: We have added the fact that FNAB was done previously (see Page 5, line 64)

Comments 4: The authors should describe how the dose of prednisolone was determined.

Reply 4: The initial dose of Prednisolone and the tapering strategy was arbitrary. However, initial high dose steroids (up to 60mg daily) are used in the suppression of inflammatory disorders in

severe disease. We chose initial dose of 40mg to minimise the adverse effect in a postmenopausal woman.

Changes in text: We have added a text to describe how the dose of prednisolone was determined (see Page 6, line 89)

Comments 5: The manuscript would be improved by a thorough English language review. There is something to write in superscript, need a space after the number, inappropriate cited journal name and so on.

Reply 5: The manuscript has been thoroughly reviewed taken into account the above comment.

Changes in text: We have reviewed the manuscript and made corrections including appropriately citing journal names and use of superscript.