AOT ANNALS OF THYROID
AN OPEN ACCESS JOURNAL PUBLISHING RESEARCH IN ALL ASPECTS OF THYROID DISEASE

Peer Review File

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Reviewer A

The followings are my comments for the case report entitled "Sclerosing mucoepidermoid carcinoma of the thyroid gland: first case in Australasia":

Comment 1

1. SMECE as a rare disease, every new case report has its own uniqueness. Readers will be very curious whether the first case in a different region has a unique appearance or disease course. I can hardly find the description in this article.

Reply 1: Thank you for your review of this case report. This case has a similar appearance and presentation to previously documented cases of SMECE. Our patient presented with a painless neck lump but additionally had compressive symptoms which are less commonly reported in SMECE.
Changes in the text: We have added a paragraph in the discussion section lines 97-103 to compare the features of this case with previously reported cases.

Comment 2

2. CT and PET were performed in this case, however, the description of the preoperative lymph node presentation is very limited. Readers need more hints to decide whether neck dissection is necessary, and whether final benign neck lymph node pathology is related to the manifestation of the disease?

Reply 2: Despite the findings of lymphadenopathy on radiological imaging the left sided neck dissection was negative for nodal involvement. Discussion regarding the finding of lymphadenopathy is that any macroscopic lymph node abnormality could be suggestive of local metastasis in the setting of cancer and should not be left in situ for the possibility it is reactive. For this reason neck dissection is necessary. From this case report we cannot comment on benign neck lymph node pathology being part of the disease process.
Changes in the text: We have added further details from the CT and PET CT reports with description of the size of the associated lymphadenopathy on lines 48-51 and 53-56. Images from the scans have also been added to the case report.

Comment 3

3. The possible extrathyroidal spread indicated on Line 45 refers to the thyroid tumor or lymph node? What kind of spread/invasion pattern? When thyroid SCC is suspected before surgery, what are the considerations for safe margin during surgery? What is the final pathology's judgment on safe margin? Is it related to the decision of adjuvant treatment?

Reply 3: The extrathyroidal spread is related to the nodule described in the left thyroid lobe. On the authors' search we have been unable to find guidelines in the literature

regarding safe margins for surgical excision of thyroid SCC. Only descriptors in the literature include clear or involved margins but do not describe what the definition of clear is. In our SMECE case, the margins were considered safe as the tumour was confined to the thyroid gland without extracapsular extension and the entire thyroid was resected.
Changes in the text: We have clarified that the ill-defined margins and possible extrathyroidal spread are described in relation to the thyroid nodule/mass on line 49-50.

Comment 4:

4. This report lacks unique viewpoints. It is only the first regional case. More detailed diagnosis and treatment details are needed. Retrospectively, is there any hint that is exclusive to SMECE and different from SCC or other DTCs, rather than just listing a rarer differential diagnosis from a rare thyroid SCC.

Reply 4: I have added extra details regarding the diagnosis and treatment of this patient. Retrospectively, the FNA described small numbers of eosinophils which would not be expected in thyroid SCC.
Changes in the text: More diagnosis and treatment details have been added to the case history section of the report. This can be found in lines 36-87. A section regarding findings exclusive to SMECE is added in the discussion section on lines 107-108.

Reviewer B

The authors reported a case of sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid gland. SMECE of the thyroid gland is a rare disease and this manuscript, which describes detailed pathological information, is considered to be valuable. Further clinical information would be useful to the readers.

Major point
Comment 1: Figures of CT, PET and ultrasonography are helpful for readers to image the tumor.
Reply 1: Thank you for your feedback. We have included images from the CT and PET CT scans in the case report section. Ultrasonography was not undertaken as part of the work up as the compressive features in the patient's presentation led to initial investigation with CT neck.
Changes to text: Figures have been updated. Figures 1 and 2 show images from radiological investigations. Figures 3, 4 and 5 are updated to the histological findings of the tumour.

Comment 2: The value of SUV max is useful to know the malignant potential of the tumor.
Reply 2: thank you this has been added.
Changes to text: SUV max has been added in the case description at line 53-54.

Comment 3: Did CT show swelling of the bilateral cervical lymph nodes?

Reply 3: there was enlargement of left sided cervical lymph nodes, the right sided nodes were not involved on the CT imaging.
Changes to text: further details regarding the CT findings have been added on lines 48-51.

Comment 4: Were there any pathological changes in the cervical lymph nodes? What was the reason for PET positive?
Reply 4: no pathological changes were seen in the cervical lymph nodes. Histological review found 0/35 nodes examined were involved. They were described as reactive in the final histology report.
Changes to the text: further information regarding histology results has been added in the case report section on lines 77-84.

Comment 5: CT findings suggest that the tumor may have invaded surrounding tissue. What were the surgical findings? Completely resected?
Reply 5: surgical findings found tethering of the anteriorly located strap muscles which were resected as part of the specimen. Berrys ligament was dissected with no obvious evidence of disease extension.
Changes to the text: a comment regarding surgical findings has been added on line 69-73

Comment 6: If possible, please present macroscopic findings as well.
Reply 6: unfortunately, a photo was not taken at the time of the surgery. There is a photo of the specimen pinned out on a cork board prior to histological examination which can be included but is not well photographed to include in a case report.
Changes to the text: -

Minor point
Comment 1: (line 32) What is MDT setting?
Reply 1: multidisciplinary team
Changes to text: thank you, this has been changed on line 32.

Comment 2: (line 36) Is ENT clinic a hospital name?
Reply 2: this is the department within the hospital
Changes to text: this has been expanded ENT to ears, nose and throat.

Comment 3: (line 48) squamous cell carcinoma(SCC), (line 74) SCC, (line 87) SCC
Reply 3: We have updated the first acronym on line 62 and all subsequent descriptors are left as SCC.

Comment 4: I don't think "Patient Perspective" is necessary
Reply 4: We have included the patient perspective section as part of the CARE guideline and checklist which asks for a section on patient perspective. We have asked the patient for these paragraphs which she has thoughtfully considered and documented. If the overall opinion is that it would be better not to include this section, we would be happy to remove it. It adds a human perspective and is always

interesting to learn what our patients' perspective is.

Reviewer C

Author described a case of SMECE, which is a very rare thyroid disease. This case report will add evidence and guide to treat patients. There are two recommendations to make this case report more informative.

Comment 1: Additional images will make this case report more informative, such as photo of patient's neck, ultrasound, CT scan (multiple images showing suspicious LN metastasis), coronal view of PET, and gross specimen. In particular, ultrasound image is essential for clinicians to understand how SMECE appears.
Reply 1: Thank you. Images have been added of the CT scan and PET scan. An ultrasound was not completed as part of the work up for the patient as her compressive symptoms of dyspnoea and orthopnoea resulted in an initial investigation of neck CT rather than thyroid USS. Unfortunately, a photo was not taken at the time of the surgery. There is a photo of the specimen pinned out on a cork board prior to histological examination which can be included but is not well photographed to include in a case report.
Changes to the text: please see the updates in the case report section including radiological images.

Comments 2: There are several case reports reporting SMECE including ones authors cited. What about making a table describing and comparing clinicopathological factors of the cases such as age, gender, clinical presentation, size, treatment, and the other factors?
Reply 2: a summary table was published in the 2017 paper "Thyroid sclerosing mucoepidermoid carcinoma with eosinophilia: a clinicopathologic and molecular analysis of a distinct entity" by Shah et al. This has a table describing characteristics and features of separate case reports of SMECE. The findings in this paper have been referenced in the discussion of our case report.
Changes to the text: findings from summary table by Shah et al. described and related to this case on lines 99-105.

Reviewer D

The authors present a case study of a rare entity, sclerosing mucoepidermoid carcinoma of the thyroid. The authors goal in presenting this interesting case was to identify potentially the first case in Australasia. The paper is clear, concise, and well written. The intention of the publication is noted. The case is clearly presented with no significant deficits. I recommend accepting this manuscript with revision.

Comment 1: First, in Line 38, the word 'medial' appears to be misspelled; perhaps the word 'medical' was intended.

Reply 1: Thank you for finding and noting this error.
Changes to the text: this spelling error has been corrected.

Comment 2: The authors mention molecular analysis with testing of BRAF and MAML2. Were any further molecular analyses performed? Why did you chose those two markers? Explaining the rationale is helpful.
Reply 2: Further markers were included in the histological analysis and I have added these to the case report. BRAF mutations have been found in cases of SMECE. MAML2 is seen in MEC but has not been associated with SMECE.
Changes to the text: We have included in the case history lines 83-84 the further genetic tests that were performed on the specimen. We have included in lines 122-125 the usual histological findings and comment on BRAF mutations. In line 147 we have noted the finding of MAML2 mutation in keeping with MEC.

Comment 3: In reviewing the discussion of the case, the authors fail to discuss how this case falls in the world literature of similar cases. I suggest that the authors incorporate data and citation from the following article to help readers understand the entity more clearly:
Shah A, La Fortune K, Miller C, Mills S, Baloch Z, LiVolsi V, Dacic S, Mahaffey A, Nikiforova M, Nikiforov Y, Seethala R. Thyroid sclerosing mucoepidermoid carcinoma with eosinophilia: a clinicopathologic and molecular analysis of a distinct entity. Mod Pathol. 2017 March; 30(3): 329-339. Doi: 10.1038/modpathol.2016.180
Reply 3: thank you for bringing this paper to our attention, it has informative and useful data and we have included this in the case report.
Changes to the text: findings from this paper have been referenced in lines: 99-104, 118-123, 138-139.

Overall, I find this article acceptable with the above recommended revisions. Thank you for bringing this case to attention and adding to the world literature on a rare entity.