Peer Review File

Article information: http://dx.doi.org/10.21037/gs-20-601.

Reviewer A

Comment 1: you must review bibliography and cite as Vancouver model.

Reply 1: We have revised the references according to the suggestion. (see Page 12, line231-260; Page 13, line 261-269).

Reviewer B

I appreciate the effort of the authors to report an interesting 2 case thyroid cancer with a dismal prognosis: angiosarcoma and myoepithelial carcinoma. It adds to the literature others cases of a rare entity. The title accurately reflects the cases. However, there are some problems that I think the authors should consider to revise. Specific comments below:

MAJOR:

Comment 1: The clinical message (the learning points) is not clear and useful. You should think that is useful to other doctors when they meet a similar situation? It is very important.

Reply 1: We have revised the text according to the suggestion.

Changes in the text: we added some data as advised (see Page 5, line 73-80; Page 6, line 106-108, line 112-115).

Comment 2: The report is poorly written however and need revision for structure and some typos as there are many concerning errors throughtout the manuscript

Reply 1: We have revised the text according to the suggestion.

Changes in the text: we have modified our text as advised (see Page 3, line 34,line 37,line 41,line 49;Page 6, line 97-98,line 101-102;Page 7, line 121,line 125,line 129;Page 8, line 149-150;Page 9, line 179;Page 10, line 184,line 186,line 189,line 196-197;Page 11, line 209,line 218;Page 12, line 224;Page 14, line 275,line 290;Page 15, line 300).

Comment 3: The authors should check plagiarism through this manuscript: for example: the sentence “Mesenchymal origin of primary thyroid angiosarcoma (TAS) is extremely rare and comprises less than 1% of primary thyroid cancer worldwide “ and “ Diagnosis of TAS is commonly made after thyroidectomy as cytologic diagnosis can be

challenging due to paucity of cells, presence of necrosis and unawareness of the disease due to rarity" were copied similarly from "doi:10.1136/bcr-2018-228862". So, please re-write these sentences and check whole manuscript.
Reply 3: "Mesenchymal origin of primary thyroid angiosarcoma (TAS) is extremely rare and comprises less than 1% of primary thyroid cancer worldwide (1)." We have already quoted the reference. "Diagnosis of TAS is commonly made after thyroidectomy as cytologic diagnosis can be challenging due to paucity of cells, presence of necrosis and unawareness of the disease due to rarity" were replaced by "The diagnosis of TAS is usually determined by cytology after thyroidectomy, which is challenging because of the lack of cells, the appearance of necrotic tissue, unawareness of the disease due to rarity."
Changes in the text: we have modified our text as advised (see Page 4, line 57-59).

Comment 4: Why were 2 patients not treated by total thyroidectomy? Total thyroidectomy is recommended if the primary tumor is 4 cm in diameter or greater, there is extrathyroidal extension of tumor, or there are metastases to lymph nodes or distant sites.
Reply 4: The first case was treated by total thyroidectomy. The primary tumor was about 53mm × 30mm × 29mm in the second case. We recommended total thyroidectomy. But the patient believed that there was no evidence of disease in the left lobe and refused to have a full thyroid excision.
Changes in the text: No.

• In the 1st case (thyroid angiosarcoma):
Comment 5: How did the authors prove this is primary thyroid angiosarcoma? Because the family refused PET-CT examination, and immunohistochemical is generally specific for angiosarcoma, not for thyroid angiosarcoma.
Reply 5: The common pathogenesis sites of angiosarcoma includes head and neck, the skin, soft tissue, retroperitoneal space, limbs, breast and internal organs. No evidence of primary malignancies or suspicious for secondary lesions was found at the preoperative routine CT of the chest, ultrasound of abdomen and pelvis. The physical examination ruled out skin lesions. So we believe that angiosarcoma in the thyroid gland was the primary malignancy.
Changes in the text: No.

Comment 6: The authors should mention the clinical features, thyroid function test ultrasonography features and FNA results. Because these features may be very important as a learning point.
Reply 6: We have revised the text according to the suggestion.

Changes in the text: we added some data as advised (see Page 5, line 73-80; line 83-84.)

Comment 7: From clinical features, ultrasound, cytological impression, the authors can add differential diagnosis of medullary thyroid cancer, anaplastic cancer, metastasis and thyroid angiosarcoma.
Reply 7: We have revised the text according to the suggestion.
Changes in the text: we added some data as advised (see Page 9, line 169-179).

Comment 8: Which did patient die from thyroid cancer or diabetes? I know this is very difficult but it shows the dismal prognosis of thyroid angiosarcoma.
Reply 8: We learn that the patient died of multiple metastases from the hands, ribs, axillary lymph nodes and lungs by contacting with his family member.
Changes in the text: we added some data as advised (see Page 6, line 102-103).

Comment 9: Was informed consent obtained from the patient or not? Was he able to give consent? This is concerning is that the authors mention that the family refused chemo or radiotherapy at the time, it is not mentioned what the patient's decision was if he is able to make his own decisions?
Reply 9: Informed consent was obtained from the patient (see Page 5, line 84-86).
The postoperative radiotherapy was recommended but it was refused by the patient (see Page 6, line 101).
Changes in the text: we have modified our text as advised (see Page 5, line 86).

• The 2nd case (myoepithelial carcinoma):
Comment 10: This is the tumor of the salivary gland, but the authors did not mention the salivary gland features in ultrasound or CT scan. So, may it be a metastasis from the salivary tumor?
Reply 10: At first, we didn't know that thyroid tumor was myoepithelial carcinoma, so we didn't check salivary gland. After pathological diagnosis of thyroid myoepithelial carcinoma, we performed ultrasound examination on parotid gland and found no abnormality.
Changes in the text: we added some data as advised (see Page 7, line 126-127)

Comment 11: The authors should mention the clinical features, thyroid function test and FNA results
Reply 11: We have revised the text according to the suggestion.
Changes in the text: we added some data as advised (see Page 6, line 106-108; line 112-115).

Comment 12: In the 1st time of treatment, I wonder why female patient did not receive any further treatment such as radiotherapy or chemotherapy?
Reply 12: After the first operation, we suggested that the patient should be treated with radiotherapy. The patients decided to take traditional Chinese herbal medicine orally, and she was not followed up on time.
Changes in the text: No.

• Discussion
Comment 13: In discussion part, the authors should describe more details about typical age of presentation, sex predominate, clinical and size feature, prognosis and cytology-Histology - Immunohistochemical studies, treatment of thyroid angiosarcoma and Malignant myoepithelial carcinomas (Review of the Literature).
Reply 13: We have revised the text according to the suggestion.
Changes in the text: we added some data as advised (see Page 8, line 157-159; Page 9, line 160-164; Page 10, line 185-186. Page 10, line 190-196; Page 11, line 215-216).

Comment 14: Differential diagnosis of medullary thyroid cancer, anaplastic cancer, metastasis and thyroid angiosarcoma is very important. This manuscript is emphasized by differential diagnosis.
Reply 14: We have revised the text according to the suggestion.
Changes in the text: we added some data as advised (see Page 9, line 169-179).

MINOR:
Comment 15: They should describe the results of intraoperative frozen pathology analysis, postoperative in line 80-83.
Reply 15: Frozen pathology in operation shows malignant tumors. A small dishesive group of large, atypical, epithelioid cells with well-defined cell borders, pleomorphic and vesicular, central nuclei and eosinophilic cytoplasms (see Page 14, line 275-278). The malignant tumor in the left lobe of the thyroid gland was found by intraoperative frozen pathology analysis. However, the characteristic has not be identified and needs conventional pathology further to diagnose. (see Page 6, line 97-99). Postoperative pathology proves to be hemangiosarcoma.(see Page 14, line 278-282).
Changes in the text: No.

Comment 16: They should describe the results of intraoperative frozen pathology analysis, postoperative in line 118-121.
Reply 16: Frozen pathology in operation shows malignant tumors (100×; H&E stain). The circular or the spindle-shaped cells were divided by fibrous septa, arranged in

small leafy or trabecular shapes， with round or oval cell nucleus and granulated cytoplasma (see Page 15, line 300-303).Therefore, the medullary carcinoma was considered (see Page 8, line 142-143).Postoperative conventional pathology proves to be recurrent myoepithelial carcinoma (400×;H&E stain). An inner layer of duct lining cells and an outer layer of clear cells, which typically form double-layered duct-like structures. (see Page 15, line 303-305).
Changes in the text: We have revised the text according to the suggestion. (see Page 15, line 301-303).

Comment 17: Please citate the references (line 128-133)
Reply 17: We have citated the references according to the suggestion.
Changes in the text: we added the references as advised (see Page 8, line 152-157).

Comment 18: Add all abbreviation in line 178
Reply 18: We have revised the text according to the suggestion.
Changes in the text: we added some data as advised (see Page 12, line 226-228).

Comment 19: Structure and some typos (space….) as there are many concerning errors throughtout the manuscript. Please check whole paper.
Reply 19: We have revised the text according to the suggestion.
Changes in the text: We have revised the text according to the suggestion.(see Page 3, line 34,line 37,line 41,line 49;Page 6, line 97-98,line 101-102;Page 7, line 121,line 125,line 129;Page 8, line 149-150;Page 9, line 179;Page 10, line 184,line 186,line 189,line 196-197;Page 11, line 209,line 218;Page 12, line 224;Page 14, line 275,line 290;Page 15, line 300).

Comment 20: Format paragraph: line 128-146
Reply 20: We have revised the text according to the suggestion.
Changes in the text: We have revised the text according to the suggestion. (see line 152-188).