

## Peer Review File

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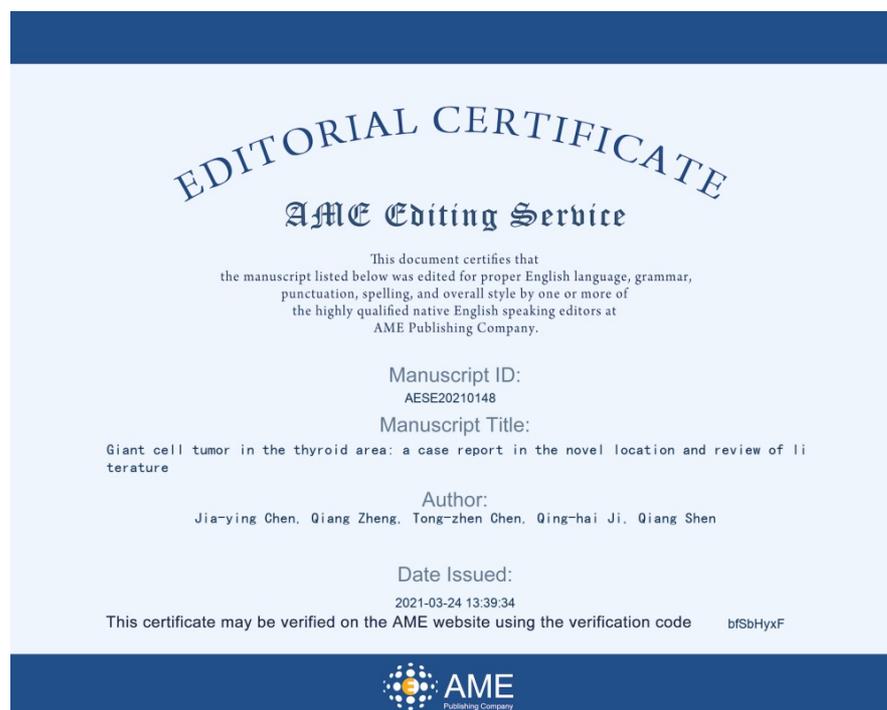
### Reviewer A:

1. Interesting presentation of a rare case of giant cell tumor in the thyroid area. Please use an anatomical nomenclature instead of e.g. "ciliary thyroid muscle".

**Reply:** Thank you for your advice. The outer layer of strap musculature includes the sternohyoid and omohyoid muscles. The inner strap musculature includes the sternothyroid muscle and more superiorly the thyrohyoid muscle. So we replace the "ciliary thyroid muscle" with the word "strap muscles" in the article, which is more specific. The related modifications were in line 29,99,100,142-143.

2. Please revise use of English throughout the entire manuscript text.

**Reply:** Thank you for your advice. Our manuscript has been polished by AME editing service so that it is free of grammatical, spelling, punctuation and other common mistakes. The certificated document was attached below.



### Reviewer B:

My comments are as follows:

1. Overall

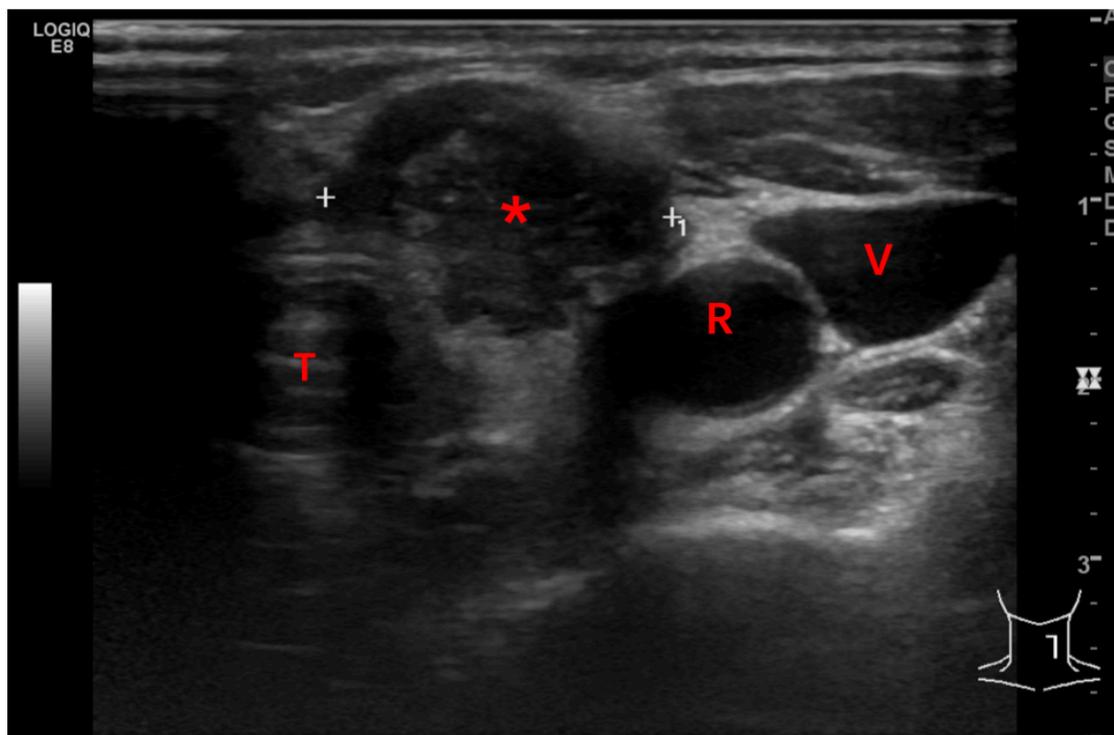
The authors describe the character of this case including the rare location result in misdiagnosis (deep neck versus superficial), rare behavior (malignant versus benign), and a new treatment trial (denosumab). However, if the authors could add the discussion on the differential diagnosis of the GCT-ST to real thyroid nodule, and the possible reason of malignant behavior of the case to the majority of benign behavior of GCT-ST, the report would appeal to more readers, and meet the scope of Gland Surgery.

Also, it may be too short to make a conclusion on the response of GCT-ST to denosumab in just three months. It would be helpful if the authors provided the response a in longer follow-up.

Questions as follows:

Line 50: Could the authors provide the neck ultrasound imaging of both the first examination and the second examination?

**Reply:** The initial exam and surgery were not performed in our center, so the authors could not provide the ultrasound image. But before the second revision surgery, the patient had a ultrasound exam in our center in late April 2020. The imaging showed the 35mm \* 28mm \* 25mm solid nodule located in the left thyroid bed. The nodule was hypoechoic with irregular margins and rich in blood flow signals. The ultrasound imaging was attached below. We modified the revised manuscript in the line 116-129 and figure 4.



2. Line 74: How long between the CT scan (Figure 4A,4B) and the first operation (February 28, 2019)?

**Reply:** The CT scan (former Figure 4a,4b, Now renumber as Figure 5a,5b) were performed in May 08, nearly 2.5 months after the initial incomplete surgery.

3. Line 132: Could the authors discuss how to avoid the misdiagnosis of GCT-ST to a thyroid nodule? What is the difference on echo appearance? Is fine needle aspiration cytology helpful for differentiation?

**Reply:** As we discussed in the text, it is difficult and even impossible to achieve correct diagnosis by sonography. The ultrasound imaging usually shows a mixed nodule with unclear margin and rich in blood supply. Furthermore, GCT is a very rare disease in head and neck region. In our patient, the tumor location and results of ultrasound initially led to the diagnosis of thyroid goiter. For the second question, fine needle aspiration had no special finding.

4. Line 148: Could the authors discuss more on how to differentiate the GCT-ST from the osteoclastic variant of anaplastic thyroid carcinoma?

**Reply:** In thyroid area, the most significant differential diagnosis of giant cell tumor is osteoclastic variant of anaplastic thyroid carcinoma (ATC). Giant cell tumor of soft tissue is composed of bland mononuclear tumor cells and osteoclastic giant cells. Unlike the former, the osteoclast-rich anaplastic carcinoma is highly aggressive. Tumor necrosis, cytologic pleomorphism and mitotic activity is usually prominent. Though tumor-infiltrating macrophages and multinucleated giant cells are frequent, the tumor cells are often highly atypical spindle or sarcomatoid cells. Vascular invasion is often present. Immunohistochemically, thyroid-lineage markers such as PAX8 is usually retained in ATC cells, whereas GCT is consistently negative for PAX8. Cytokeratin is usually negative in GCT, expression of cytokeratin supports the epithelial nature of ATC, while negative staining of CK could not totally exclude the diagnosis. We added relative discussion in the revised manuscript in line 309-318.

5. Line 170: Could the authors provide more information of the repose of GCT-ST to denosumab in a longer follow-up?

**Reply:** Thank you for your advice. The patient had a CT scan after 3 months of denosumab ,showing the significant decrease of the anteroposterior diameter from 5.7cm to 4.4cm (Figure 7A-7D) . Due to the COVID19, the patient didn't not come to our hospital but had a CT scan in the local hospital after 1 year treatment of denosumab in the late December 2020. The patient demonstrated symptom-relieving. CT scan showed the tumor lesion were stable. The anteroposterior diameter was 3.7cm after 1 year of denosumab (Figure 7E,7F) . We added relative data in the revised manuscript in line 38-39, 239-243 and figure 7E 7F.

6. We advise adding a description icon on the imaging to help the reader understand the important finding in the imaging.

**Reply:** Thank you for your comments. We added relative description icon on the fig 1,4 and 6.