

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dear Author(s), Please make the following changes to the article: 1/ The title of the article should be altered to be more descriptive of the study, as the title implies that the paper is a case report and literature review, but in reality, the paper is more of a case report than a review.

Answer: In this article, we report one case with granular cell tumor of the breast from our hospital. Meanwhile, a careful study of the literature was performed to comprehend this rare disease. May I ask if you have a better suggestion for the topic? I will be very appreciated.

2/ Based on the basic criteria for writing the study's abstract, the abstract of the study requires more work than what occurred in this paper.

Answer: The abstract is revised as follows: Granular cell tumor of the breast (GCTB) is a rare neoplasm that can exhibit malignant characteristics clinically and radiologically, as well as coexist and colocalize with breast carcinoma. We present a case with this uncommon tumor and discuss the diagnostic and therapeutic approaches in order to further knowledge of GCTB and prevent misdiagnosis and overtreatment. The characteristics, methods of diagnosis, therapy and postoperative pathological outcomes were analysed, and relevant literatures of granular cell tumor were reviewed. This patient underwent surgery after core needle biopsy, and the excised neoplasm was sent for pathological examination. Histological analysis revealed nests of cells with abundant pink granular cytoplasm, confirming the diagnosis of GCTB. As manifestation of the disease and malignancy can mimic each other, a careful histological examination is an essential process before major operation.

The treatment of complete excision with close clinical follow-up is recommended.

3/ The study's introduction is relatively brief and irrelevant to the research question in its current form. It is advised that the study introduction be rewritten in three paragraphs as follows: The first paragraph of the study introduction should express the significance of the current study, the second paragraph should express the knowledge gap that the current study seeks to fill, and the third paragraph should express what the problem of the current study is and how it can be solved within the framework of the study's goal.

Answer: The introduction is revised as follows: Granular cell tumors(GCT) were firstly described by Abrikossoff in the year of 1926.^[1] They can occur in any body site, commonly reported in the skin, oral cavity, digestive tract, and subcutaneous tissue. The overall incidence of granular cell tumors in surgical specimens was 0.03%.^[2] Involve the breast in 15% of cases.^[3] 1% to 2% of these lesions can be malignant, with poor prognosis and few curative options beyond operation.^[4] Granular cell tumor of the breast(GCTB) can mimic breast carcinoma clinically, radiologically, making it difficult to distinguish from breast malignancies. In order to improve the understanding of GCTB and prevent misdiagnosis and overtreatment, we report one case with GCTB, who was admitted to our hospital. A brief study of the literature was performed for comprehend this unique disease.

4/ Are the photos from photo 1 to photo 4 truly owned by the patients in the current study, or were they obtained from other sources? I hope that if this is the case, you will protect the third party's property rights to avoid any future disputes in this area.

Answer: The photos from photo 1 to photo 4 truly owned by the patient in the current study, and I have already add the copyright information(Copyright ©Yan Jun 2023) to the bottom right-hand side of the picture in PowerPoint.

All graphs or text portions can be reprocessed by the editor.

5/ The final paragraph of the discussion section should be updated to clarify the current study's strengths and shortcomings, as well as the current research's future directions.

Answer: The final paragraph is revised: In this article, we describe a rare breast neoplasm that had radiologically indicatives of a malignant tumor but was later determined to be a benign granular cell tumor of the breast following extensive local excision. Complete imaging analysis and biopsies could be of significant assistance in making diagnosis and avoiding invasive procedures. After review of the literature, clinical trials and gene research are still required for a deeper knowledge of this rare condition.

6/ The author(s) must revise the conclusion in light of whether the current study met its objectives, that is, if the current research topic was solved or not.

Answer: The conclusion is revised: In conclusion, granular cell tumor of the breast is a rare disease and can often resembles breast cancer. In the present case, the patient had imaging characteristics of malignant tumors, the histology points to benign lesions. A thorough imaging evaluation and core needle biopsy are necessary prior to beginning a major operation. Complete excision to negative margins with close clinical follow-up is gold standard treatment strategy for GCTB at the moment. Clinical trials and objective molecular data before treatment initiation are needed for deeper knowledge of malignant GCT and the development of effective treatment.

7/ Some references are out of date and should be updated. References from 2023 and five years prior are required.

Answer: Totally agree. I have already add some articles published recently. Since granular cell tumor is very rare and there were limited valuable articles, I decide to keep some older articles.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors:

1. This is a very significant case, and there is a poor development in women, so it is of great significance to arouse widespread concern.

Answer: Thank you for your encouragement.

2. Since histology is involved in the case report, and S100 and other positive cases are also mentioned, can we show the report of this part of the immunohistochemical study?

Answer: After review more studies, the following paragraph will be added: It used to be widely accepted that GCT is derived from the Schwann cells of the peripheral nervous system due to the presence S-100 protein^[5]. Additionally, GCT could also stain positively for CD68, neuron-specific enolase, vimentin, CD57, CD56, SOX-10 and inhibin.^[1, 6, 7] However, a subset of S100-negative “non-neural” granular cell tumors have been identified.^[8] The histogenesis of GCT is still debatable at this time.

3. Since it has been mentioned in the literature that the incidence in women is higher than that in men, and that the incidence is high between 40 and 60, is there a deeper explanation for this?

Answer: The corresponding expression will be amended as follows: All age groups and genders can be impacted. In general, GCT are almost twice as common in women as in men, affected patients are predominantly in their fourth to sixth decades.^[2, 3, 9] 1% to 2% of these lesions can be malignant, with poor prognosis and few curative options beyond operation.^[4] Granular cell tumor of the breast(GCTB) is largely a disease of females as is the case in breast malignancies, but has been reported also in the male population,

accounting for 6.6% of all GCTB cases.^[10] GCTB frequently resembles malignant neoplasms clinically and radiologically, making it challenging to identify from breast cancers. More references were added.

4. In the article, the author mentions that there is no other good treatment for the GCTB except surgery, including chemotherapy. Let the author further elaborate. What is the main reason why her chemotherapy is ineffective? Is there an immune escape mechanism, or is there any other reason? Is there any literature report in this regard? Please ask the author to supplement the explanation.

Answer: The corresponding expression will be amended as follows: Since Pazopanib has been approved for advanced soft tissue sarcomas through a phase III trial, pazopanib for metastatic soft-tissue sarcoma (PALETTE), there were several cases demonstrated response in patients with malignant GCT. Due to the overexpression of multiple genes by the tumor and multiple targets of agents, it is difficult to establish the mechanism of action responsible for disease response through limited cases. Clinical trials and appropriate cell lines or mouse models are essential to ascertain the exact mode of action responsible for tumor response.^[22-26] More references were added.

5. According to the literature cited by the author at the end, we can see that the 5-year survival rate of GCTB is very low and the degree of malignancy is very high. Why does this very high degree of malignancy occur? Can the author describe this aspect and provide more information, which is very helpful to readers?

Answer: The prognosis for benign GCT is excellent. Patients with malignant GCT, however, have a worse prognosis. Malignant GCT had an overall cause-specific survival rate of 74.3% after 5 years and 65.2% after 10 years, respectively. Patients with tumors larger than 5 cm had a worse chance of

survival (90.0% vs. 51.3%, respectively; $P = 0.02$) than patients with tumors smaller than 5 cm. The prognosis was much worse for those who had regional or distant metastases at the time of diagnosis.^[27] In this article, 5-year survival rate of malignant granular cell tumor of breast with tumor larger than 5cm, local lymph node metastasis or distant metastasis is very low.