Peer Review File

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Reviewer A

I have noticed that the age and tumour volumes have been calculated as mean. I prefer calculations to be performed as median instead of mean. Apart from that everything else seems fine.

Reply 1: Thank you for your helpful advice. We have added the median age and tumour volumes to Table 1 and listed both the median and mean values for a more intuitive and reliable presentation. Changes in the text: In lines 221-223, the Results section: “There were 26 TGCT samples (8 diffuse TGCTs and 18 localized TGCTs), 16 SC samples, and 11 SS samples from patients with median ages of 54.5, 62.0, and 24.0, respectively.” More detailed changes were made and are shown in Table 1.

Reviewer B

This is a single institution, retrospective study that aims to summarize clinical, histologic and molecular features of 3 rare synovial lesions that provide a diagnostic challenge: tenosynovial giant cell tumor (TGCT), synovial chondromatosis (SC) and synovial sarcoma (SS). Ability to differentiate between these 3 lesions is very important as correct diagnosis is needed to choose most appropriate therapeutic approach and educate the patient about prognosis. The analysis suffers from very small patient numbers as only 26 patients with TGCT, 16 patients with SC and 11 patients with SS were included. Given very small patient number and retrospective nature of this analysis, which is prone to cofounding factors and bias, the results are difficult to interpret. Given rarity of these diseases, prospective studies are not likely to be undertaken since accrual would be very slow. It seems to me that a better approach here

would be to collaboratively combine patient numbers from multiple institutions together to increase the statistical rigor and impact of this work. Nevertheless, the authors should be congratulated on their hard work to perform very extensive analysis which showed that pain was the presenting symptom of TCGT and SC and growing mass was a presenting symptom of SS. Younger patients and increased neutrophil to lymphocyte ratio and increased expression of CD163 was associated with higher risk of recurrence of TCGT. No specific clinical or pathologic prognostic factors were identified for SC and SS. Comment 1: Was the association between CD163 staining and recurrence based on initial diagnosis (i.e. high CD163 expression on diagnostic specimen was associated with higher risk of recurrence)? Based on figure 3, strong CD163 staining was seen in the "recurrent" tumor but not on the "non-recurrent" tumor. If the staining at diagnosis is weak but increases when malignancy recurs, then the clinical value of this test is less compared to association of CD163 expression at baseline and risk of experiencing TGDT recurrence.

Reply 1: Thank you for your insightful comments. We are sincerely sorry for causing this confusion. All specimens included in the study were from initial tumor resection. No recurrent tumors were included. The association between CD163 staining and recurrence was based on initial diagnosis. High CD163 expression in the resected specimens indicated a significantly increased risk for recurrence. We have revised the Methods section to clarity and further explain the associations in the Results section according to your kind reference. Changes in the text: In lines 175-177, the Methods section: "All specimens included in the study were from initial tumor resection. No recurrent tumor specimens were included in the further staining analysis." was added. In lines 281-282 in the Results section: "The association between CD163 staining and recurrence was based on initial diagnosis." was added.

Comment 2: Was your study approved by institutional ethical board (such as Institutional Review Board or an IRB for example)? Did the patients who participated in this retrospective analysis provided an informed consent. If that was not the case (for

example waiver of consent was obtained from the local ethical board), please explain this.

Reply 2: Thank you for your helpful advice. This study was approved by the institutional ethical board of the Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine. The approval number is SH9H-2019-T163-2. We have added the relevant information to the Methods section. Individual consent for this retrospective analysis was waived.

Changes in the text: In lines 178-181 in the Methods section: "This study was approved by the local ethics committee of the Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine (No. SH9H-2019-T163-2), and individual consent for this retrospective analysis was waived."

Comment 3: The sentence in line 109-111 of the introduction: "Long-term surveillance may be appropriate for benign TGCTs and SC, but for SS, a malignant tumor, early intervention is highly recommended for a high metastatic ratio." The meaning is unclear. Did the authors mean to state: "…but for SS, a malignant tumor, early intervention is highly recommended for a high metastatic potential." (?)

Reply 3: Thank you for your valuable advice. We have corrected this sentence to make it clearer.

Changes in the text: In lines 133-135 in the Introduction section: "Long-term surveillance may be appropriate for benign TGCTs and SC. However, for SS, due to its malignant nature, early intervention is highly recommended for its high metastatic ratio."

Comment 4: A sentence in line 191-192 in the Results section states the following: "Patients who were diagnosed with SS were younger than the patients in the other two groups, with an average age of 1.15±2.90 years." Based on table 1, age of mean patients with SS was 28.6 years. I am unsure where 1.15 ± 2.90 came from?

Reply 4: Thank you for your helpful suggestion. In this sentence, the “1.15±2.90 years” represents the disease duration before diagnosis. We have changed this sentence and replaced it with a better statement.

Changes in the text: In lines 226-227 in the Results section: “Patients with SS had the timeliest diagnosis in hospital among the three diseases, with an average disease duration before diagnosis of 1.2±2.9 years.” The data in Table 1 were also changed accordingly.

Comment 5: Consider carefully editing the manuscript by an English-speaking person.

Reply 5: Thank you for your important advice. We have requested revisions from the editing service AJE (the verification code is ED6B-E550-2F73-1682-3B00), who have corrected errors related to spelling, grammar, and word choice in the manuscript. The editing certificate is provided in the Supplementary Materials.

Changes in the text: We have changed several errors and misleading statements according to the suggestions of the editors from AJE.