Peer Review File

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Reviewer A

Congratulations for the good work produced. It certainly offers hints and confirmations for further studies. I am in favor of publishing after a minor revision in language and wording.
I find the references adequate.

Reply for Reviewer A: Thank you for your consideration of this manuscript and for the thoughtful revisions you provided to help improve this manuscript for publication. We made some small changes in language and wording that we hope you find sufficient and beneficial to the paper, while maintaining the previous message of the work. One of the first changes we made was a formatting issue in which we had to bring down the abstract to a new page to leave space for a title page (see line 41). We made some edits to the "Key Findings" portion of the abstract (See below line 61 on page 2). We changed the grammar in the Introduction (see lines 71 and 72 on page 3). We changed the heading of "Data Collection and Synthesis" to "Data Synthesis and Analysis" (page 4, line 108). We made some changes to phrasing on page 4 on the lines 112, 117, and 118. We also removed unnecessary info on page 12, line 187 and added important info regarding tumor diameter on page 12, line 195. Finally, we made some edits to the conclusion on page 14, lines 280-282 and 289 that more accurately depicts our findings.

Changes in the Text:

-Page 2: Added lines on title page to move abstract down to page 2

-Page 2, "Key Findings" Table:
- **-Replaced "Women developed more cases of UPS in the chest than men" with "There are more reported Cases of UPS in the chest for women than men"**
- **-Replaced "Radiation-Associated UPS was found in 5 of 22 patients that developed the tumor secondarily" with "Secondary development of UPS was associated with radiation in 5/22 patients"**
- **-Replaced "worsened" with "worse" and "that have" with "with"**

-Page 3:
- **-Line 71: Replaced ";" with ", so"**
- **-Line 72: Deleted "further"**

-Page 4:
- **-Deleted space between paragraph (line 99 and 100)**
- **-Line 109: Replaced "Collection and Synthesis" with "Synthesis and Analysis"**
- **-Lines 110 and 116: Replaced "was" with "were"**
- **-Line 112: Replaced "from" with "from these cases"**
- **-Line 117: Added "(NS)"**
- **-Line 118: Added "as this would likely be reported in the case"**

-Page 12:
- **-Line 187: Removed ", as discussed below"**

-Line 195: Added "(>5 cm diameter)"

-Page 14:

-Line 280-281: Replaced "more… have been found to have UPS tumors involving the chest than men" with "are more case reports of women with UPS of the chest wall"

-Page 15:

-Line 289: Replaced "Is primarily found in the trunk as well" with "more commonly found in the trunk as well"

Reviewer B

The manuscript submitted completely reads as a standard review/mini-review, not a systematic review. In addition to the significant weaknesses and aversions in including case studies and series in systematic reviews, the authors boldly set out to answer multiple questions, instead of a single question that is characteristic of the approach of a systematic review. The authors somewhat address this in the Methods section (line 106), but consequently disqualify the systematic review and the analytic approach which provides its foundation. The discussion, while well written, reads mostly as an extended summary of UPS and sarcomas in general, before touching on some of the individual cases and reviews. Even then, this can be accomplished in a mini-review, but this is not a systematic review.

Reply: First, thank you for your thoughtful comments and for providing insight that can be used to potentially improve our review. In response to your comments, we broke it into subsections that we believe have different recommendations, so we can better address each one specifically in these responses.

With that stated, we first wanted to address your comments on this being similar to a standard review/mini-review. While we do agree that this is similar to a standard review, we felt there is not a ton of guidance on surgical recommendations and consolidated information on undifferentiated pleomorphic sarcoma of the chest wall (such as outcomes, adjuvant therapies, margin distance, etc.). Therefore, we elected to use a systematic review to help identify important literature to include when discussing possible treatment guidelines. Moreover, there is relatively little information about this cancer type appearing in the chest wall region, especially in the realm of random controlled trials. Given the lack of literature on this subject, we elected to use case reports and case studies to help consolidate some information about these tumors for researchers to access. In selecting literature, we felt that we needed to apply some structure - via a PRISMA framework – to improve methodological protocols beyond just a random selection of pertinent cases and series.

It should also be noted that our work was intended to be a systematic review without meta-analysis, given the constraints that are placed on case reports/series in these types of reviews. We did not want to draw statistical conclusions as we do not feel as though we can use cases to do so. This was intended to allow us to provide possible future directions for research and offer more insight into this space without misdirecting future researchers.

We do believe that we insufficiently address this in our review, as you have noted. Therefore, we made some changes to the paper to improve upon this aspect. We added another sentence to further address this in the methods section and explain why a systematic review process (and the PRISMA framework) was used (see page 4, lines 129-131). We also added a paragraph in the discussion that answers this as well (see page 14, lines 257-263).

Changes in Text:

-Page 4, lines 129-131: Added

"Third, an intended goal of this review was not to draw statistical conclusions but to provide researchers with cogent topics to analyze in a more controlled setting by systematically selecting literature."

-Page 14, lines 257-263: Added

"For the purpose of this study, a systematic review was performed with the intention of qualitatively selecting literature for the purpose of providing a cogent direction for future researchers to focus on when considering this entity. Given its rarity and the minimal empirical work done to draw strong conclusions regarding the surgical treatment of this type of tumor, this work was supplemented with information from case reports and series to help fill in some of these gaps. We elected to follow a systematic approach to help keep cases relatively consistent in terms of the presented information in those studies."

Finally, the second to last paragraph of the discussion (starting line 180) is a mixture of results and discussion, with a somewhat random Chi-squared test mentioned and discussed (though this was not mentioned in the Methods).

Reply: This is a strong point considering the lack of value that the Chi-Squared test provides, so we are really appreciative of the insightful respond to improve our manuscript. As such, we moved the majority of this paragraph to the results section and then made another paragraph in the discussion that addresses the comparative aspects. We also discussed the chi-squared test in the results and methods, so thank you for pointing out that mistake on our part (see page 4 lines 132-134 for methods). For the results change, see page 5 from lines 146-162. For the changes to the discussion, see pages 13-14 with the addition of lines 219-236 and the removal of lines 237-255.

Changes in Text:

-Page 4 Lines 132-134: Added

"A chi-squared test of independence was performed comparing patients who received therapy versus patients who did not receive therapy to see if there was any association with recurrence or metastasis. The programming language, R, was utilized to perform these assessments."

-Page 5, lines 147-163: Added

"*Findings*
Table 1 reveals some metrics that may be interesting to consider given our current understanding of UPS. First, 8/32 (25%) of the patients identified in our review of trunk UPS were male. Additionally, 24/32 patients (75%) had tumor diameters greater than 5 cm in one dimension.

In terms of treatment, 17/32 (53.13%) received some form of adjuvant or neoadjuvant therapy. Of these 17 individuals, 6 (35.3%) still developed distal metastasis or local recurrence. Comparatively, 6/10 (60%) that had follow-up information and no adjuvant therapy reported metastasis or recurrence. The chi-squared test results revealed that there is no connection between therapy application and the occurrence of metastasis or local recurrence ($\chi^2 = 1.56$, df = 1, p = 0.2122).

For patients who received adjuvant or neoadjuvant chemotherapy, 5/13 (38.5%) experienced some form of recurrence or distal metastasis, with the liver and lungs being the primary locations. For patients who received neoadjuvant or adjuvant radiotherapy, 2/8 (25%) had local recurrence or metastasis. Furthermore, 6/16 (37.5%) of surviving patients with tumor diameter greater than 5 cm in one dimension had local recurrence or metastasis, and 2 were noted as dying of their disease. 5/22 (22.7%) with a UPS of the breast had a radiation-associated malignancy as well."

-Pages 13-14, Lines 220-263:

-Replaced the results/discussion paragraph with:

"In regards to the results, there are a few limitations that are important when considering these results. As stated prior, these are case reports and case series of a rare phenomenon, so there is likely some selection bias. As such, there were more reported cases of females with UPS of the breast than males. This outcome could be explained by a few factors with greater selection of female patients, sex-related differences in tumor location, or difficulty identifying tumors early in women due to the proximity to breast tissue. Furthermore, 75% of the patients had a tumor size greater than 5 cm in 1 dimension. Given that 24 of the patients were female, difficulty in noticing small masses in the chest and a lack of notable symptoms could allow tumors to grow >5 cm without being detected.

The Chi-Squared test of independence noted no association with recurrence or metastasis and whether the patient received other therapies. However, these are case reports and not random controlled trials, so it is difficult to draw conclusions relative to current literature without proper experimental methods.

Current literature suggests that radiation-associated UPS occurs in 5.2% of UPS cases, but these case reports demonstrate an occurrence of 5/22 for secondary malignancies (22.7%).(61) Consequently, this may further support current evidence that radiation-associated UPS is more commonly found in the chest than other parts of the body, but this data needs to be taken likely given the nature of the reports."