Author's response to reviews

Title: Peripheral Giant Cell Granuloma with Extensive Osseous Metaplasia, or Hybrid Peripheral Giant Cell Granuloma-Peripheral Ossifying Fibroma: A Case Report

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Author's response to reviews: see over
The Biomed Central Editorial Team

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**Title:** Peripheral Giant Cell Granuloma with Extensive Osseous Prosoplasia, or Hybrid Peripheral Giant Cell Granuloma-Peripheral Ossifying Fibroma: A Case Report

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**Author’s response to reviews:** see over
Thank you for your Consideration of our manuscript for publication in your journal.

We have reviewed the above manuscript according to your reviewer’s comments, and changes related to the reviewers’ recommendations are highlighted in yellow.

Referee #1 (Professor Odukoya)

MINOR COMMENTS:

1. “How objective is your assessment that the PGCG and mineralized areas of the histopathology of the case being reported of near equal proportion?”

   We thank the Reviewer for their insightful observation and suggestion. Our assessments were purely subjective estimations, based on light microscopic evaluation of the histologic sections, without the application of any matrix to achieve precise proportionality. While a more objective method that involves other parameters may be necessary in a case series study, the purpose of the current case presentation is to enhance the debate on the possibility that some of these cases may represent true hybrid lesions.

   [P1]: “Remove”

   Done

   [P2]: “POsF”

   Done

   [P3]: “Why did you consider this despite observation of absent radio-opacity?”

   We reasoned that radio-opacity is not always apparent in conventional soft tissue radiograph

   [P4]: “If you had impression of benign lesion, this bit should be discarded.”

   We retain the practice of including malignant differential diagnosis where the possibility exists, albeit remote. We consider this case one of such where that ‘element of surprise’ is a possibility.

   [P5]: “is this abbreviation correct?”

   No. We apologize for the typographic error and have now corrected this in the manuscript.

   [P6]: “Was there an objective assessment of this proportion?”

   Please see response to (1) above.

   [P7]: “POsFs are reactive lesion”
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Now corrected in the text

[P8]: “PGCGs are reactive lesions”

Now corrected in the text

[P9]: “We recommend that more cases of hybrid P0S/P/GCG be reported in the scientific literature”

We have incorporated (with modifications) the suggestion of the Reviewer, and sincerely thank the Reviewer for their suggestion, which will greatly enhance the quality of this manuscript.

Referee #2 (Dr. Bello)

MINOR COMMENTS:

1. “Is the use if the term prosoplasia justified? This reviewer does not believe so. Prosoplasia has been originally defined as forward differentiation of cells or groups of cells to a higher level of function or organization. It is still not well understood which cells are making mineralized products in this lesion. Even if the latter appellation is accepted, changing from fibroblasts which are able to make collagen to cells which are able to make osseous products is still within the same range of differentiation. This is probably better termed as metaplasia because of functional or reactive needs of the cells, if the term is to be used at all. Moreover, a great number of workers believe that the mineralized products are derived from cells originating in the periodontal ligament. So it is confusing what the term ‘prosoplasia’ is being applied to here. Most well-known pathologists have always used “osseous metaplasia” for this type of presentation (i.e. if they even consider using the term necessary in the first place) as it would be more defensible even if the nature of the lesions are not completely understood. If the authors feel otherwise, then it will be better to discuss this clearly in their discussion section. They have not been explicit enough about the entity undergoing the osseous prosoplasia.”

We thank the reviewer for their insightful observation and suggestion. We agree with the Reviewer and have accordingly replaced the word “prosoplasia” with “metaplasia” as suggested in the title and all aspects of the manuscript affected.

2. ‘The term “hybrid tumor” used in the abstract is probably more appropriate for the central lesions which are tumors and are frankly quite unrelated to each other histogenetically. For the peripheral lesions, hybrid tumor (or even “hybrid lesion”) is difficult to justify especially when the etiology is basically the same (reactive to some traumatic or irritating factors) and many workers believe these lesions are just different expression of the same process. The picture seen is more of a reflection of a number of factors including patients own physiology, age of the lesion, extent and constancy of irritating factors etc. This reviewer suggests that any allusion to “hybrid tumor” is significantly downplayed or even removed altogether. The authors should not try to fix this lesion like a jig-saw puzzle replica of their reported corresponding “hybrid”central lesions. Again, the authors should provide a convincing reason(s) that this is a hybrid tumor or even lesion than as presently provided.’

We again thank the Reviewer for their comments. We agree with the Reviewer that the respective central “namesakes” (Central Ossifying Fibroma and Central Giant Cell
lesions/Tumors) of the peripheral lesion we are presenting are believed to have different histogenesis. However, the term “Hybrid”, as used in the abstract in the current report on Peripheral Ossifying Fibroma and Peripheral Giant Cell Granuloma is meant to elicit debate as to the possibility that current dogma, that both entities are a spectrum of the same disease, may no longer hold in cases such as the current where “differentiation” towards two clear morphology appears to be quite apparent. The attempt here is certainly not to “to fix this lesion like a jigsaw puzzle replica of their reported corresponding “hybrid” central lesions” but to revisit the current concept with the possibility that the existing dogma as to the histogenesis of two peripheral lesions may not hold true in all cases. We have used the phrase hybrid “lesion” instead of hybrid “tumor”, and believe this to be consistent with our view of this case.

3. “In this reviewer’s opinion, this lesion will be diagnosed by some pathologists based on the authors’ description simply as “peripheral giant cell granuloma with extensive osseous metaplasia” or “peripheral ossifying fibroma with extensive giant cell accumulation” As already conceded by the authors in the manuscript, in lesions like this the dominant portion determines where the pathologic diagnosis goes. This reviewer believes that it should be the case as it probably has no bearing whatsoever on the management and prognosis of the lesion. One of the strength of the manuscript is that it appears to be well written although it appears to stretch the simple towards the complicated.”

Although these lesions are regarded as a spectrum of a single disease process, the possibility that they may not have previously been implied. For example, the fact that Dayan et al (Ref. 12) emphasized the absence of cementum deposit in “peripheral ossifying fibroma with extensive osseous metaplasia” as a basis for characterizing these lesions as such, instead of true hybrid lesions, speaks to recognition of the possibility of hybrid lesions in cases meeting the Dayan criterion. Even though we disagreed with this sole criterion (see Discussion) cases meeting this criterion may not be uncommon. For reasons detailed in 2 above, we believe that this case presentation should enhance the discussion of a possibility of some of these lesion representing true hybrid lesions as is the case with their central counterpart.