

Author's response to reviews

Title: Carcinosarcoma of the colon: report of a case with morphological, ultrastructural and molecular analysis.

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Author's response to reviews: see over

Dear Alexander Pemberton,

We are hereby submitting you the revised manuscript titled “Carcinosarcoma of the colon: report of a case with morphological, ultrastructural and molecular analysis” by Ambrosini-Spaltro A et al. We thank the reviewers for their comments and we have included several changes that we feel have improved the content of the manuscript.

Specifically we wish to respond point by point to the observations made, as follows:

Reviewer 1: no observations.

Reviewer 2:

1. We have not obtained the photograph of the surgical specimen at the time of the initial evaluation. This is because the diagnosis of carcinosarcoma was not known at the time, and we do not obtain macroscopic pictures of all cases as a routine procedure.
2. The clinician planned a palliative procedure for what was preoperatively considered a routine case of carcinoma occurring in an old patient. For the same reason liver biopsies of the metastatic foci were not performed.
3. Unfortunately it is not known why capecitabine may have been particularly effective in this case. We have specified in the manuscript (page 5, last paragraph of clinical features) the reason to use this agent. We have also included a new reference (reference 3) to this effect.

Reviewer 3

1. The point that the polymorphisms reported are not a formal proof of clonality is well taken, although of course they certainly are not against it. Therefore we have conserved in the report the description of these polymorphisms, and in addition we have evaluated a new set of microsatellite markers on chromosomal arms 9p, 11p, 13q, 17q and 18q. We found an LOH on 18q in both the neoplastic components. This result supports the common clonal origin of the epithelial and the mesenchymal components of the tumor.
This additional result has been included in the Abstract (case presentation section), in the materials and methods section, in the results section, in the discussion section and conclusions. A figure displaying this new result has also been added (Fig.6).
2. As discussed in the observations for reviewer 2, point 2, due to the palliative nature of the surgical procedure, the liver biopsy was not performed. Although a formal proof that the masses in the liver are metastases, this is the most reasonable interpretation. Therefore we have not changed the manuscript in this regard.

Overall, the following formatting changes have been included:

1. Patient consent has been added in the Acknowledgements paragraph
2. The “Abbreviation list” paragraph has been removed since acronyms are explained within the text
3. Fig 6 has been included as well as text explanation for microsatellite analysis.
4. One reference [3] has been inserted for comprehensive answer to Referee 2, question 2.

We thank you for the thorough review of our manuscript and hope that the revised paper is now acceptable.

Best regards

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